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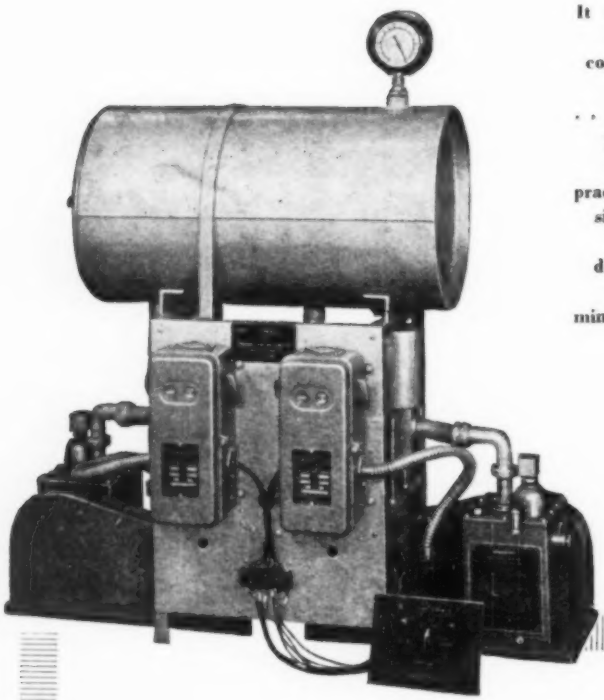

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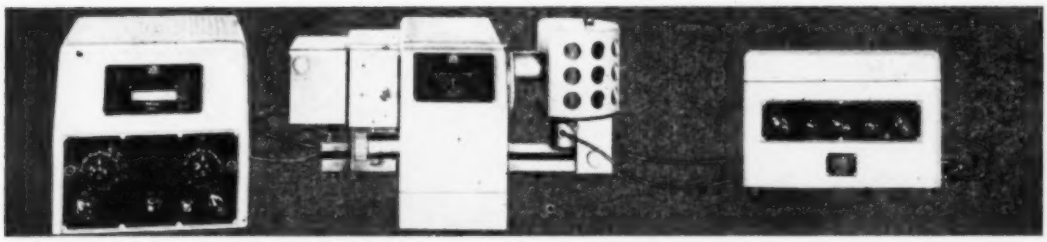

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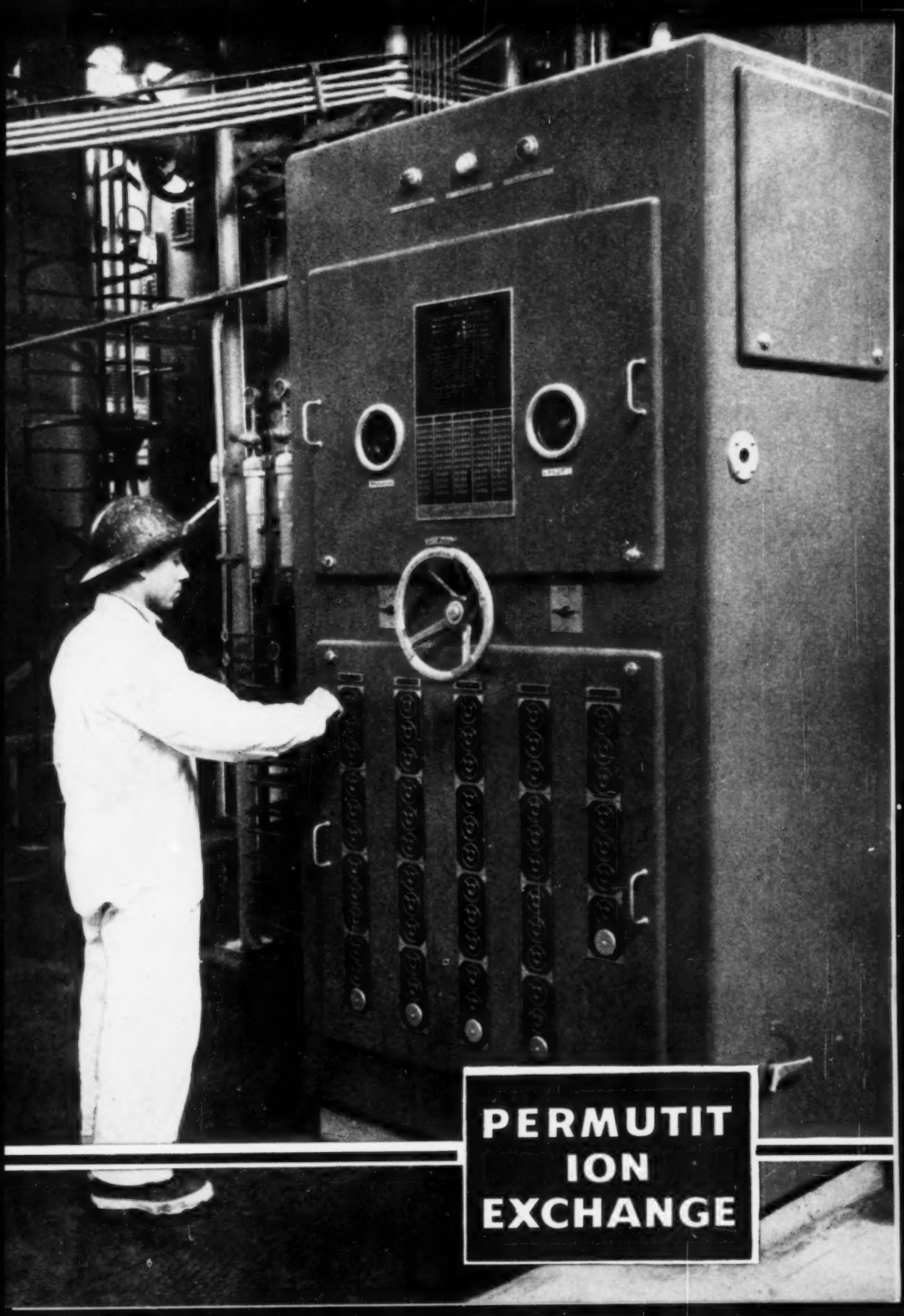
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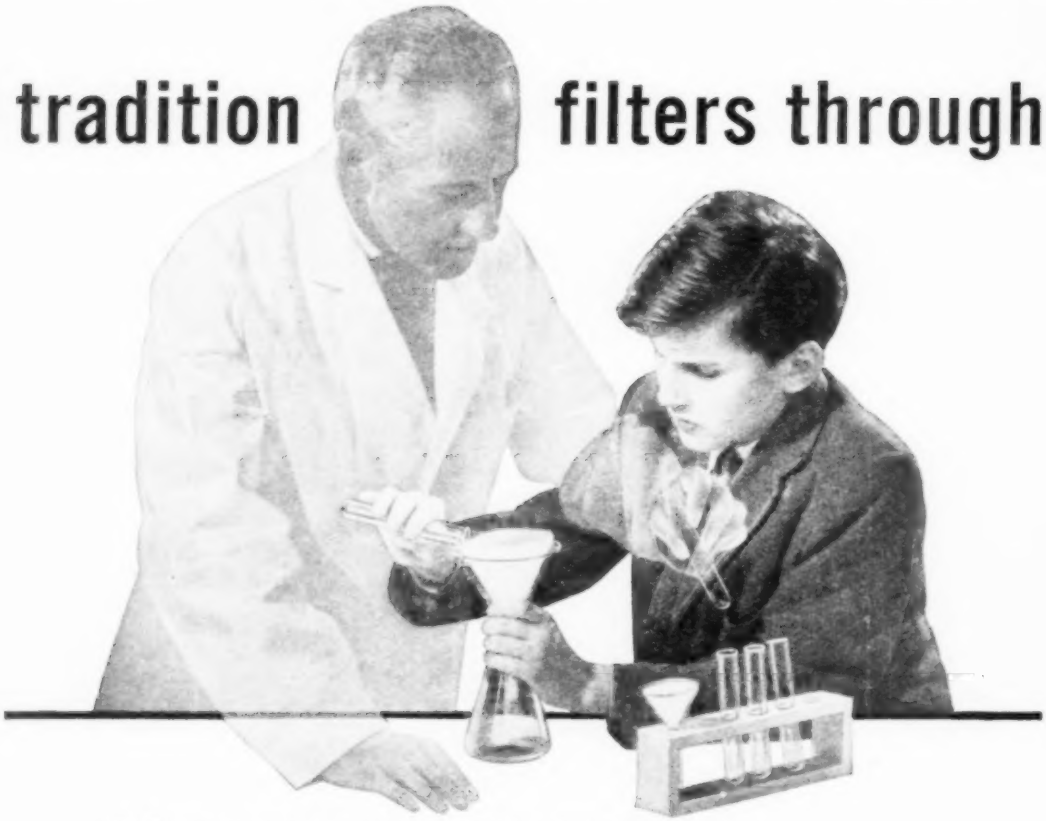

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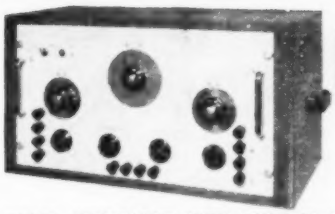

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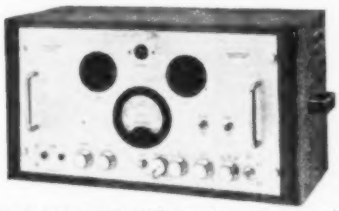

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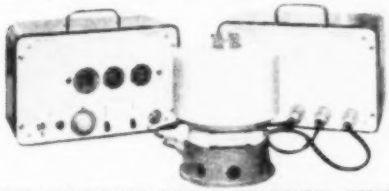

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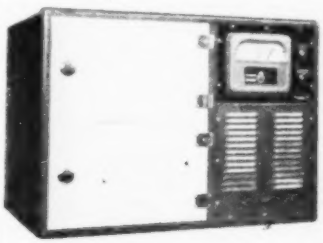

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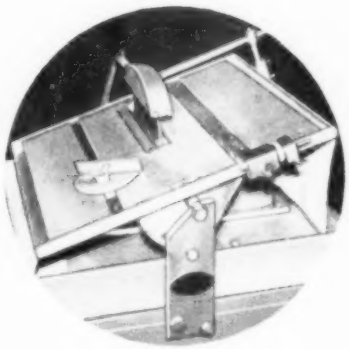

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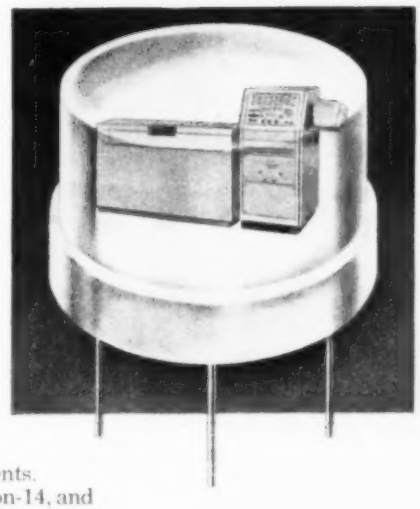

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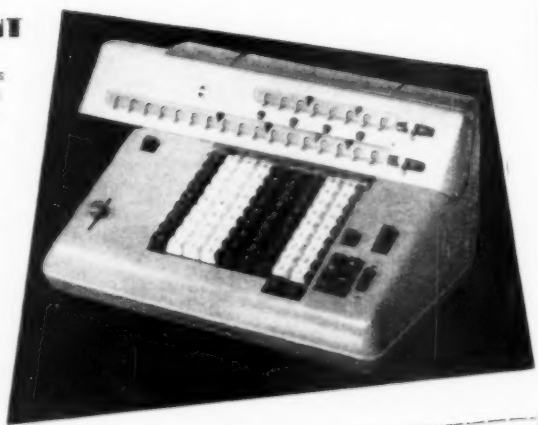

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CONSERVATION OF NATURAL RESOURCES

ONE important gap in responsibility revealed by the review of scientific effort in Britain made by the Advisory Council on Scientific Policy at the request of the Minister for Science relates to the conservation of natural resources—minerals, land use and biological resources. The responsibilities of the Nature Conservancy cover only limited aspects, and as its annual report shows (see p. 798), even these are interlocked with the responsibilities of other Departments, which may or may not be responsible to the Minister for Science, as well as with the interests and responsibilities of various public or private bodies. The Advisory Council was satisfied that there is a significant absence of basic research in such major problems as the conservation and long-term utilization of water-supplies in Britain, while in formulating the considerations on which policies of land utilization should be based, much remains to be done towards a scientific classification of land capability, including the application of soil science and comprehensive topographical investigations.

On these subjects the Advisory Council is continuing its discussions with the authorities concerned, and meanwhile a study of the competition for rural land by Dr. G. P. Wibberley, of the Department of Agricultural Economics, Wye College, shows the value of research on land reclamation and the need for further effort in this field. The Advisory Council also stressed the need for study of the effect of long-term climatic changes on policy for the conservation of resources, and in view of its suggestion that the application of research in tropical ecology would facilitate the economic planning and execution of development schemes for under-developed countries, it is particularly disappointing to find that the recent report, *Colonial Research 1959–60*, contains no hint that the Overseas Research Council is addressing itself with any vigour to the problem of providing continuity of research in tropical agriculture and medicine in the emergent territories of the Commonwealth. Generally, however, the Advisory Council believes that the conservation of natural resources may be of sufficient importance to justify establishing a research council with central responsibilities, to ensure that, over the whole field, scientific knowledge and research are brought to bear on all these issues; the problem is being considered in detail by the Biology and Allied Sciences Committee of the Council. This suggestion for a further research council found some support in the debate on scientific policy in the House of Lords on November 9, though Lord Shackleton thought that in the first instance the functions and responsibilities of the Nature Conservancy might be extended to enable it to do the work. Lord Hailsham did not specifically reject this suggestion, though he pointed out that the Agricultural Research Council is also working in this field and he thought that we should first have a very clear idea of how any new research council would fit into the general scheme and what sort of work it should be asked to undertake. These matters will doubtless be elucidated by the Advisory Council's sub-committee which is considering the problem; in the meantime the Nature Conservancy states in its annual report that it is already most carefully considering a number of recommendations made by the Advisory Council on subjects of importance to the conservation of natural resources of Britain.

The Nature Conservancy's annual report, however, brings out once again not only inherent inadequacy on the part of the Conservancy to deal with such matters but also the inadequacy of the resources at its disposal. Its grant-in-aid for 1959–60 was no more than £336,000, and after providing some £205,000 for staff and £91,000 for properties and equipment, only some £44,231 was spent on research, training and special surveys, of which £21,509 was in research grants and £14,021 on studentships and training grants. It is scarcely surprising that applications for studentships or for places in the postgraduate diploma course in conservation should far exceed the number of awards the Conservancy is able to make, and the urgent need in conservation for recruits of high calibre to lead and inspire the growing movement of naturalists' trusts continues. Again and again the report refers to fields in which available information is inadequate, but in which no systematic efforts are yet being made to supply the lack; and it is obvious that the directions in which, with its present resources, the Conservancy can increase its efforts are severely limited.

More scientific and technical knowledge about the coast of Britain is needed, and the natural forces and threats affecting it; and on developments here the report quotes as still relevant the judgment two decades ago of the Coastal Preservation Committee, that the question how amenities and facilities shall be designed, where they shall be sited and how the essential characteristics of the coast and the adjoining landscape can be saved from destruction in the process, is urgent and vital in the absence of national control. In this particular field the Conservancy is promoting a fresh survey of the preservation of the coastline of England and Wales, but the report concludes with the judgment: "Almost every day brings new evidence of the price of our present methods of pursuing economic progress. Poisoning of wild life, pollution of seas, shores and rivers, destruction of irreplaceable scientific and amenity features and the exposure of vulnerable flora and fauna to excessive and unreasonable human pressure are among the current threats with which conservation must contend".

Part of the story of the struggle is told in the report, and the Conservancy's hope that enough of the picture will be made plain to awaken public opinion before it is too late should be widely shared by scientists, not least because of the way in which scientific interests themselves have been sacrificed. The picture, however, is not entirely black, and before referring more particularly to the glaring example of Dungeness, some of the encouraging features noted in the present report should be mentioned. First and foremost are the clear signs that the need for conservation, and the efforts of the Conservancy to that end, are becoming better understood and more widely accepted. This is notably true among the universities, as is illustrated by the support given by the University Grants Committee, which enabled the first advanced training course in conservation and ecology to be initiated at University College, London, and by the agreement of the University of Aberdeen to the establishment of the Conservancy's first research unit dealing with grouse and moorland ecology. The Welsh headquarters of the Conservancy and Research Station, opened at Bangor last July, is a notable addition to scientific institutions in Wales; its equipment includes an X-ray vacuum fluorescence spectrograph for elemental analysis of soil and plant material which will greatly reduce the time taken in analysis. An experimental station is also being planned on a site adjoining the Monks' Wood Nature Reserve; this will house the scientific group being formed to study problems of chemical spraying in relation to wild life and also other groups undertaking research on woodland management by natural methods in natural areas, the ecology of vertebrates (particularly mammals and birds) and scientific methods of conservation.

The high esteem for British progress in the field of conservation was manifest when many overseas scientists attended the celebration of the tercentenary of the Royal Society; this event was preceded by a meeting and tour of the British Commonwealth Scientific Committee, in the course of which the heads of all the principal Commonwealth scientific departments visited the Conservancy's Merlewood Research Station, while in June leading workers in this field were entertained and consulted on their way to attend the meetings in Poland of the International Union for the Conservation of Nature and Natural Resources. Evidence of Government interest in conservation was also seen in the promptness with which the Minister of Education acted on a recommendation of the Albemarle Committee and made a grant to the Council for Nature to enable the Conservation Corps to be expanded. The report again pays tribute to the value of the Conservation Corps in easing the difficulties due to the present shortage of field-staff in the reserves.

These and other events have all assisted to create a better-informed public opinion; and the Nature Conservancy has made its own direct efforts to that end. To assist the reconciliation of public access with scientific research and conservation, the Conservancy, in May 1960, signed an agreement with the Hampshire County Council under which the latter undertook to assist, so far as it properly can, towards the preservation of Old Winchester Hill and to help ensure that its extensive use by visitors does not cause injury or disturbance to this fine view-point or to its plants and animals and the studies which are being made of them. The Conservancy has also taken the initiative in seeking compromises or efforts of reconciliation between conservation and other interests in various areas where conservation is threatened by pressure of growing population, and in particular, promising informal discussions have taken place on the preservation of the coast-line.

Reference has already been made to the bearing of the Conservancy's work on wild life and agriculture overseas. The Government's concern for wild life in Africa was explicitly affirmed by the Colonial Secretary in the House of Commons last June, when he said that wild-life conservation measures are continuously under review in the East and Central African territories, but that more use could be made of technical knowledge in developing the wild-life resources, which contribute considerably to local food supplies, as well as being of economic value to the tourist industry. He recognized also the voluntary co-operation of the African populations, and welcomed the prospect of a conference on conservation in Africa being convened in 1961. The deputy-director-general (scientific) of the Conservancy, Dr. E. B. Worthington, has already submitted to the Colonial Secretary a full report on his extensive tour of East and Central Africa during February 7–March 19, 1960, and his report emphasizes the critical importance of conveying to the masses of the indigenous African people the economic importance of the conservation of African wild life and of securing the interest of their leaders. It also indicates the real assistance which the Nature Conservancy can give both in the application of technical knowledge to local management problems and in the training of staff.

Meanwhile, at the meeting of the International Union for the Conservation of Nature and Natural Resources held in Poland, an African Special Project was accepted as a major activity of the Union during the next three years. This project, which is to be launched in close co-operation with other international agencies, aims particularly at influencing African public opinion towards the conservation and wise use of natural resources, including wild life. Nor, as the report shows, are the overseas functions of the Nature Conservancy limited to Africa or to wild animals.

There are thus wider reasons than domestic ones why every care should be taken that the Conservancy's resources in finance, in staff and equipment are adequate to fulfil the increasing responsibilities which fall on it. Apart from the time factor stressed by the chairman in his report, Britain's scientific prestige is to some extent now involved by the new overseas commitments; and it should be a matter of urgency that the Minister for Science should satisfy himself not merely that adequate resources are

available to the Conservancy, but also that the administrative structure is appropriate, including the relations with the Overseas Research Council and the Agricultural Research Council.

Nor is it simply a matter of adequate finance. Government interest must be much more positive than in the past. The Nature Conservancy is dissatisfied, for example, with the protection afforded by Sites of Special Scientific Interest status, and is examining, through discussions with the National Parks Commission, the Council for the Preservation of Rural England and other bodies, the possibilities for improvement. Too often, while sites may be protected against building or other forms of statutory development, the scientific interest is damaged or even obliterated by planting of trees, draining or ploughing, since forestry and agricultural development are not subject to planning control. Moreover, in conservation as a whole, there are still difficulties in assessing with sufficient precision for management purposes the scientific significance of an area.

The gravest threats, however, still come from the Government itself, and the Conservancy's comments on the Dungeness decision make most disturbing reading. In view of the decision announced in July 1959 to authorize a nuclear power station within the boundaries of the proposed reserve at Dungeness, the Conservancy decided not to proceed with the proposed reserve in view of the severe loss to the scientific interest. In announcing this decision on November 24, 1959, the Conservancy said that study of the direct and indirect repercussions of the power station on the remaining area showed that the future scientific interest would be too much reduced to qualify it for the status of a national reserve. The undeveloped area will remain 'designated' as a site of special scientific interest, and the Conservancy will continue to be consulted about any future development which may be proposed for other parts of the area; and in particular it will welcome and encourage any measures which the Royal Society for the Protection of Birds may take for maintaining and defending the fauna and flora, and especially the bird life of the 1,234 acres of shingle which it owns between the power station site, the Lydd Army Ranges and the bungalow settlement.

Nevertheless, as stated at the public inquiry, the issue was that of a clear choice between the conservation of the unique natural interest of Dungeness for scientific research and education, and the exploitation of the area as an engineering site. What is disturbing is that, after scientific interests have been irredeemably sacrificed—and interests which were unique and irreplaceable and could have supplied information of the utmost importance in coastal defence work generally—it should appear that this sacrifice of an important national interest was not really necessary. As the Conservancy's chairman points out in this report, the nuclear power programme has since been revised and it has been decided, for example, that a station on the Wylfa site in Anglesey, approved as suitable, will not be required in the period up to and including 1966.

This possibility was pressed by the Director-General of the Conservancy at the public inquiry at Lydd in December 1958, when he asked if there were not a risk that the nuclear power programme might not be revised again in such a way that the authorization for the site at Dungeness might prove unnecessary. The Chairman of the Conservancy very rightly remarks in the present report that the frequency with which sites of the highest scientific or amenity interest are claimed on grounds of over-riding priority, when experience shows that the reasons given are quite frequently modified even before construction takes place, is a national problem which deserves further attention. The Nature Conservancy recognizes the difficulties of averting such situations; but it does not consider that all possible methods of anticipating them and of minimizing the resultant harm have yet been explored. Its report is submitted to the Minister for Science and refers to a number of matters which call for the Minister's particular attention. None, however, is more important or more urgent than that emphasized in this comment on the Dungeness decision, and it is of over-riding importance that the Minister should take every possible step to ensure that there is no repetition of the Dungeness blunder. If sacrifice of unique and irreplaceable scientific and national interest is demanded, the possibility of doing so in deference to ephemeral requirements should be absolutely excluded. Revision and alternatives should be sought first and not after the sacrifice has been made.

TRANS-ANTARCTIC EXPEDITION 1955—58

Trans-Antarctic Expedition, 1955–1958
Scientific Reports. No. 2: A Gravity Traverse of Antarctica. By J. G. D. Pratt. Pp. 22. 12*s.* 6*d.* net. No. 3: Seismic Soundings across Antarctica. By J. G. D. Pratt. Pp. 69. (London: Trans-Antarctic Expedition Committee, 22 Gayfere Street, S.W.1, 1960.) 30*s.* net.

THE accomplishment of the Trans-Antarctic Expedition as a feat of human endeavour has rightly taken its place alongside the notable journeys of Antarctic history. The first scientific reports by the Expedition's geophysicist, J. G. D. Pratt, have now been published. The work was carried out under very difficult conditions of travel and climate, and early delays during the journey due to crevasses meant that less time was available for scientific work while crossing the plateau than had been anticipated. The amount of work done under these conditions is impressive.

Report No. 2 on the gravity programme deals at length with the performance of the Worden gravimeter. After correcting for the somewhat variable drift of the instrument, the raw gravity results are presented. No calculated gravitational anomalies are given, since the necessary heights above sea-level will not be computed with sufficient accuracy for gravity reduction until appropriate International Geophysical Year weather analyses over the Antarctic continent

become available. The author's estimate of possible errors of up to 5 milligals in the raw results seems reasonable. In view of the expected precision of the final elevation measurements, the gravimetric data should be satisfactory for determining the regional anomalies if sufficient measurements of ice thickness are available. Smaller relative errors between adjacent gravity stations should also be satisfactory for giving finer details of sub-glacial relief. A small section on the vertical motion of floating pack-ice and ice shelves, as estimated by the use of the gravimeter, is a useful side-line to the main programme.

Report No. 3 deals with the seismic shooting measurements of ice thickness. The interest of most readers will be centred on the six pages plus one sample seismic recording which deals with reflexion shooting during the crossing of the Antarctic plateau. The difficulties of operating complicated electronic equipment under onerous conditions were clearly overcome. However, the discussion of techniques and the amplitude of the echoes in comparison with the noise-level on the sample record from the South Pole show that much could have been gained had the Expedition been able to take efficient power-drilling equipment on the crossing, so that the seismic shots could have been fired at depths of 20–30 m. or more. This had been shown to be very desirable by similar work on the Antarctic plateau by the Norwegian-British-Swedish Antarctic Expedition, 1949–52. Pratt concludes that the use of greater shot depths is the most promising single line by which improvement of results may be attained, and recommends that equipment to drill to 50 m., if not 100 m., should be carried in future.

The selection for publication of a seismic record obtained at the South Pole could not have been bettered if publication of only one record was practicable. The record is stated to be of typical quality; in due course it is hoped that it can be compared with those of shots fired by two other expeditions at the same point. Pratt marks two weak echoes on his record, the first at an uncorrected arrival time of 1·021 sec., the second at 1·438 sec. The first echo is used to determine the depth of ice at 1,990 m. This compares with a Press report of a depth of ice of about 2,500 m. obtained by Linehan (United States) shortly before Pratt's arrival, and a depth of 2,810 m. obtained by Kapitza (U.S.S.R.) in December, 1959, and published in a paper by Dralkin (*Priroda*, No. 10, 27, 1960). There is no reason for preferring Linehan's preliminary result to Pratt's value, since both were obtained with shot-depths less than 10 m., but since Kapitza fired his shot at a depth of 50 m. one is inclined to prefer his result. If Pratt's second echo (1·438 sec.) is taken to come from the bottom of the ice, it would give a depth in agreement with Kapitza's value. I would agree with the clear discussion of the possibility of errors in picking echoes from the sub-glacial floor, except that Pratt discounts the possibility of noise on the record being mistaken for the required reflexion, as may have happened in this case.

Clearly those interested in measurements of the thickness of ice who are not specialists at seismic shooting will wish to know why different individuals produce different answers for ice depths at one point. On the outer parts of the Antarctic continent, where ice temperatures are above − 30° C., it is not difficult to produce first-class results from most areas of inland ice. Some fully reliable results have also been produced on the Antarctic plateau, and there is no doubt that the overall picture of great depths of ice over much of Antarctica is correct. However, under noisy shooting conditions on very cold firn, echoes may not show up clearly against the noise, or a double reflexion may show up when the first reflexion is obscured. Some risk of error clearly arises under these conditions. One can hope to eliminate most errors by making sure that data from seismic soundings, gravimetric measurements, surface slopes of the ice sheet and perhaps magnetic measurements are consistent with one another. The preliminary results of the Norwegian-British-Swedish Antarctic Expedition 1949–52 on the depths of floating ice-shelves had to be reviewed on such a basis. A similar revision of ideas of the thickness of the ice at the U.S.S.R. Vostok station has taken place (Kapitza found a thickness of 3,700 m. compared with an earlier seismic shooting value of 1,800 m.). It is apparent that we shall get the best value from the Trans-Antarctic Expedition results only after a thorough comparison of gravitational anomalies and surface slopes with the possible seismic echoes has been made. It is therefore hoped that when the final report on gravitational anomalies is prepared, such a reassessment of all the data will be made. It will also help the individual research worker if more of the reflexion records obtained while crossing the plateau can be published at the same time.

The remaining fifty pages of the report cover work of more specialized interest on refraction shooting at South Ice, and an extensive analysis of the methods and errors involved in determining the thickness of the ice shelf near Shackleton by use of strong reflexions from the sea bottom.

Pratt writes clearly with a rather informal style which shows a healthy disrespect for established ideas that do not have a firm basis. No bibliography is included in either report. The format, printing and general production of the reports are of high quality.

G. DE Q. ROBIN

SAHARAN ETHNOGRAPHY

Tribes of the Sahara

By Dr. Lloyd Cabot Briggs. Pp. xx + 295 + 33 plates. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1960.) 32*s.* 6*d.* net.

ACCORDING to Dr. Briggs, "More pure balderdash has been written and repeated about the tribes of the Sahara than about almost any other peoples in the world". In *Tribes of the Sahara* he sets out to correct this, and to show that "the sober truth about the Sahara is more mysterious than anything that has been written about it". But the Sahara is essentially a French literary possession and the mystery and romance which it evokes in French writers disappear when reduced to arid Anglo-Saxon prose. It changes into a mirage of unstable, unattainable hypotheses, and the reader finds himself abandoned in a shifting sea of desiccated gritty facts—that a camel's rate of water elimination is "less than a third of the average figure for mammals in general" (p. 28); that the underground aqueducts locally known as 'foggaras' 'may have been introduced" into the Sahara by the Persians (p. 12); that the best Touareg sword-blades "were imported from Northern

Italy, Germany and Spain" (p. 149); that their kinship structure gives "the distinct impression of a double descent system" (p. 134); that the "sedentary women of Metlili go without trousers as a rule" (p. 208).

The book falls between two stools. It has far too many 'scientific' facts of this sort to make it a successful travel book; on the other hand, there are far too many theories and insufficient supporting data to make it acceptable to anthropologists, archaeologists or historians. Human geographers, however, should find it very useful, for it answers their need for a descriptive summary of the peoples of the Central and Western Sahara which is both up to date and accurate, and which takes care to distinguish between fact and fantasy. That the latter still occupies so much space is not a reflexion on Mr. Briggs's scholarship but on the weakness of anthropological fieldwork in this part of Africa. One could have wished, however, that he could have spent less of his twelve years of study in "threshing and winnowing all the Saharan literature that he could lay his hands on", and more time in field research among the Chamba and other representative communities.

The book is supported by two very inadequate sketch maps, thirty-three good plates and an impressive bibliography. G. I. Jones

THE ECOLOGY OF AFRICAN GAME

Wild Life in an African Territory

By Dr. F. Fraser Darling. (A Study made for the Game and Tsetse Control Department of Northern Rhodesia.) Pp. viii + 160. (London: Oxford University Press, 1960.) 25*s*. net.

THIS book is primarily a report of a survey carried out by the author in Northern Rhodesia, with the object of examining the present status of the wild African game, the natural vegetation where it survives and the problems involved in the conservation of wild Nature in this territory. Much of the book is thus an account of the journeys undertaken and the terrain examined, followed by an ecological description of the vegetation and the habitats. The book concludes with an account of the measures of nature conservation already undertaken by the Government, and with recommendations for future action. There are, in addition, three appendixes, a directive on wild-life conservation issued by Sir Evelyn Baring as governor of Kenya, an official circular issued to all provincial commissioners in Northern Rhodesia on the same subject, and finally, a paper dealing with the status of the more important ungulates in Northern Rhodesia.

These materials are largely matters of record, though they give an excellent idea of the present condition of the country, and are valuable as a record and for comparison with such earlier data as are available.

In many ways the most interesting part of the book is the relation of this material to the underlying philosophy, and to the reflexions and observations embodied in the introduction and the middle chapters in which the ecology of African biological communities is discussed. Here the author draws freely on his wide experience to generalize. His view is that many of the existing habitats and biological communities in undeveloped Africa represent ecological climaxes which yield the maximum biological production possible under the difficult climatic and ancient soil conditions prevalent. This is mainly because the organisms present include a multitude of highly adapted plants and animals, the diversity of habit and function of which exploits to the full every variety of ecological niche. It follows that a disturbance, and especially a simplification, of the ecological system (such as follow human 'development') is almost certain to lead to degradation of production and to site deterioration. There is therefore a case for maintaining the existing habitats and wild-life systems until further inquiry may disclose methods of land-use which can be fully equated with the natural systems already existing.

Dr. Darling applies this generalization to the particular problem involved in the conservation of the ungulate African animals and their habitats, including the human societies involved in his treatment of this eco-system. He considers that the game can be conserved and also used to give an adequate supply of protein food for Africans in the territory and this, rather than known alternative forms of land-use, offers the best prospect of preserving rather unstable habitats and also perhaps of permitting time for the development of the primitive human social systems. He has succeeded in integrating his material so well as to give a valuable picture of the background and the relation between social life, land-use and ecology in the still savage parts of Africa. Thus the book is an important and useful illustration of the new scientific approach to these problems of wild-life management as well as to the ecology of land-use. W. H. Pearsall

KINETIC THEORY OF GASES

Elements of the Kinetic Theory of Gases

By Prof. E. A. Guggenheim. (International Encyclopedia of Physical Chemistry and Chemical Physics. Topic 6: The Kinetic Theory of Gases, Vol. 1.) Pp. xii + 92. (London and New York: Pergamon Press, 1960.) 17*s*. 6*d*.

THIS is the first part of the *Encyclopedia of Physical Chemistry and Chemical Physics* to be published. It leads us to expect an outstanding work.

Treatments of the kinetic theory of gases have tended to fall into two classes: there are the comprehensive, detailed and somewhat involved accounts which are concerned to be rigorous, regardless of complexity, and, on the other hand, there are simple, approximate accounts, frequently using unsatisfactory assumptions. *Elements of the Kinetic Theory of Gases* seems likely to make a wide appeal to readers who find neither of the two classes satisfactory.

A skilful mathematical formulation of basic kinetic phenomena leads to treatments of successive topics which are both incisive and concise. Clarity is furthered still more by the organization of the material into virtually self-contained, short chapters. The result is that the reader is continually struck by the power of essentially simple procedures which penetrate to the core of a problem, as, for example, in the derivation of Maxwell's distribution law. Again, collision-rates are considered with rigour but without complexity. Simplicity is not shunned even where

rigour is lacking, provided it affords insight. The naive treatment of viscosity is given, though to be sure it is followed soon enough by an account which does not assume Maxwellian distribution of velocities; there are parallel treatments of thermal conductivity. On the other hand, no attempt is made to include simple theories in the sections on diffusion and thermal diffusion.

In the final chapters on gas imperfections and intermolecular forces, the fashionable 6–12 potential function is severely scrutinized, and the difficulty of obtaining inter-molecular potential functions from second virial coefficients alone is exposed. A synthetic five-parameter function is advanced and shown, for argon, to give an impressive account of the dependence on temperature not only of the second virial coefficient but also of the entropy, heat content and density of the solid.

The book is aimed at graduate and research workers, but the mathematical treatment is such that undergraduates in their final year could profitably read much of the earlier and later chapters of the book. It is not only part of an encyclopaedia to be consulted and referred to, but also a book to be read and enjoyed.

D. J. Millen

INVISIBLE LUNATIC

Automatic Translation

By D. Yu Panov. Translated from the Russian by R. Kisch. Edited by A. J. Mitchell. Pp. vii+73. (London and New York: Pergamon Press, 1960.) 21*s*. net.

Automatic Language Translation

Lexical and Technical Aspects, with particular reference to Russian. By Prof. Anthony G. Oettinger. (Harvard Monographs in Applied Science, No. 8.) Pp. xix+380. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1960.) 80*s*. net.

THE title of this review is prompted by the story, until recently apocryphal, that a Russian computer translated the phrase "Out of sight, out of mind" from the English and that an American machine, in due course, re-translated the Russian back into English with the above result.

In so far as this story has a point, it is illustrated by the two books under review. Both are the first generally available technical reports produced by mechanical translation workers in their respective countries. By saying this I do not in any way mean to neglect the volumes of brief essays which have already appeared or the excellent reports, of limited circulation, which some American groups have issued.

Both books describe the activities of single groups of workers, and both are coloured by the particular machines used for the experiments.

Panov's book starts by discussing how human beings go about the act of translation, and then, after examining the characteristics of scientific and technical prose, describes the electronic computer *Besm* 1 and experiments made with its aid in this field. Detailed programmes are analysed and there is a critical survey of the present theories of translation.

Oettinger follows similar lines, except that his machine is the *Univac* 1, and that he is far less concerned with translation theories than with the precise details of Russian–English dictionary construction.

On balance it is fair to say that Panov's book will be far more readable to the non-specialist and, correspondingly, far less useful to workers in the field. Oettinger's book is nearly five times as long and is packed with useful data for the specialist.

Both books are excellently written and can be thoroughly recommended.

A. D. Booth

ALL ABOUT MANGOES

The Mango

Botany, Cultivation, and Utilization. By Dr. Lal Behari Singh. (World Crops Books.) Pp. xiii+438+54 plates. (London: Leonard Hill (Books), Ltd.; New York: Interscience Publishers, Inc., 1960.) 84*s*. net.

IT is pleasing, as it is unexpected, to find a new series of books on world crops starting off not with such solid fare as wheat or potatoes or cabbage but with something as exotic and appetizing as the mango. This "choicest fruit of Hindoosthan" has spread far beyond the bounds of India and has become one of the most cherished fruits of tropical lands. It is still found in greatest variety and excellence in India, and this book comes, fitly enough, from the pen of a distinguished Indian horticulturist.

The book may be counted on to commend itself as the most complete study of the mango so far published. There has indeed been a recent book, also entitled *The Mango*, which splendidly described the Indian varieties, but had only a short account of their cultivation. Dr. Singh deals with the subject on a broader front, concerning himself not only with the botany and requirements but also with propagation and management, the diseases and pests to be withstood, and the uses to which the mango is put.

While the botanical chapters refer mainly to the common mango, *M. indica*, the author directs attention to fifteen other species of *Mangifera* with edible fruits. Evidently there is great wealth of related material here, of possible value for future breeding. A clear and well-illustrated account is given of methods of vegetative propagation. In describing the practice of cultivation, the author is strangely insistent that the established orchard needs ploughing twice a year to maintain a proper soil tilth. It is not clear why such a disturbance is preferred to maintenance of a more natural leaf-litter. The section on utilization is necessarily brief, since the best way to use a mango is still to eat it as promptly and as dexterously as possible, but some mango recipes are also given. A full bibliography and a good index complete the work.

The book could have done with some tidying up, for misprints and some not quite lucid passages occur. In striving for completeness, the author tends to length, and his more impatient readers may grudge the space given to explaining what a horticultural variety is, or the detail spent on different methods of applying irrigation water to a tree which, over much of its range, is satisfied by the rain from heaven. In giving such full measure, the author doubtless errs on the right side, and his book deserves to be welcomed and to be gratefully added to the small, but growing, collection of hand-books on the tropical crops.

T. A. Russell

A TURNING POINT IN THE STUDY OF INSECT MIGRATION*

By Dr. J. S. KENNEDY

Agricultural Research Council Unit of Insect Physiology, Entomological Field Station, 34A, Storey's Way, Cambridge

C. G. JOHNSON[1] has crystallized a new trend, since the War, in the field of insect migration and dispersal by flight. The trend is inspired largely by work on aphids and locusts, which has been more intensive than that on economically less-important insect migrants such as butterflies. The new knowledge gained cannot be fitted into the previous framework of behavioural ideas due to C. B. Williams[2–4]; therefore Johnson (working on aphids) and Rainey[5] (on locusts) propose shifting the emphasis to the timing and results of migration. This would mean abandoning, along with his particular ideas, Williams's general aim: to characterize migration ecologically, behaviourally and physiologically. The purpose of this article is to suggest that the recent advances, far from giving cause to abandon that aim, have brought it within reach.

Records of migrating insects other than locusts have been collected and collated for many years under the leadership of Williams, and the outstanding achievements of this work are: the demonstration that migration is much commoner than was supposed, even if we count only the long-range and geographically clear-cut cases that Williams considers; and secondly, the detection of apparent return movements in an ever-growing number of species. Lack of evidence of any return in many cases had previously posed a problem of the evolutionary origin of the migratory habit and lent colour to the idea that migration served mainly to reduce high populations[6]. But in all the observations so collated the chief criterion used for distinguishing insects as migrant is the peculiarly persistent, undeviating manner of flight of butterflies, dragonflies, locusts and other large powerful fliers when close to the ground. This gives them a mysteriously purposeful air that rivets the attention of observers and makes teleological interpretation almost irresistible. This in turn proved an impediment to the development of the subject on the physiological and ecological sides alike.

Williams inferred that such migrants continue to fly low, holding to one compass direction for hours and days on end, and in this way directly determine the route of their long-distance movements. This has recently been disproved for locusts and questioned for some butterflies[7], and has not yet been verified for any insect. But taken as fact it posed an intractable problem of the mechanism of orientation. Williams even suggested that migrants had an innate sense of direction independent of the environment. There the matter of direction determination has rested, while other physiological problems of migration have remained in the background.

Furthermore, only insects flying in that self-propelled, self-directed manner were regarded by Williams as migrants. The dispersal of smaller, weaker, more buoyant insects such as winged aphids or moth larvæ that drift on the wind, merely supporting themselves by their wing beating or on silken kites, was not migration. Williams's definitions of migration are to be understood in that exclusive sense: "a change of location which is determined both in distance and direction by the insect itself, and not a passive distribution of individuals by overpowering forces such as strong winds"[2]; or "movement determined by the insect itself; [which] instead of being haphazard in direction, is straightened out so as to result in a change of habitat"[4].

Movements that result in a change of habitat are, of course, of major concern to ecologists[6,8,9]. They, however, regard regular long-range to-and-fro movements between discrete areas as special cases. Hence all the work done on such migration has seemed of doubtful relevance to everyday ecological work. Ecologists use the looser term 'dispersal' for the general phenomenon in which they are interested, and Elton's[8] description of dispersal as "taking place all the time as a result of the normal life of the animals" seems quite the opposite of Williams's basic idea of migration as a distinct biological process. In the absence of more information on dispersal mechanisms, ecologists who do believe there are distinct behavioural 'adaptations for dispersal', have had difficulty in describing them objectively[9].

Recent Advances

Locusts and aphids have, in the past, served as excellent illustrations of the supposed contrast between active migration and passive dispersal. But it turns out that locusts migrate on the wind no less than winged aphids: and winged aphids are, in their own way, no less specialized as migrants than locusts. Both are active, 'deliberate' migrants: and both achieve their long-range movements 'passively'. This is what has made a broadening of the idea of migration seem pressing[1,5].

The new phase opened in the locust work (mainly on the desert locust, *Schistocerca gregaria* Forsk.) when it was realized that the orientation of fliers and the direction of their long-range migrations were separate problems: the one did not directly determine the other[10,11]. The explanation of their purposeful air when seen flying close to the ground does not lie in any type of orienting stimulus capable of maintaining a fixed course and track for long periods. It could be explained in terms of familiar types of orienting stimuli from the immediate environment. These have a steadying effect on courses and tracks near the ground, but certainly do not fix them. For example, low-flying locusts,

* Based on papers contributed by the author to symposia on migration at the eleventh International Congress of Entomology, Vienna, August 18, 1960, and at the Anti-Locust Research Centre, London, September 22, 1960.

like butterflies and aphids as well as locust 'hoppers' migrating on foot, change course away from upstanding objects and so keep in the open where locomotion can be maintained. Non-migrating insects frequently turn toward such objects and are arrested.

But low-level oriented flying achieves relatively little displacement over the ground. The more important way in which the swarming locusts' behaviour ensures that they travel is by their rising actively away from the ground and, moreover, allowing themselves to be lifted by convection, like aphids. In this way, they not only avoid obstacles (including such obstacles as the Atlas Mountains) but also pass out of range of any optomotor orienting effect of the ground pattern and ride the faster-moving upper air. Then, the only obvious orientation reactions are those of locust to locust counteracting the disruptive effects of air turbulence on the swarm. Groups of locusts within it show a common orientation, but this varies from minute to minute and group to group. Cohesion is maintained only because any group that approaches the edge of the swarm, on any side, turns back into it. Meanwhile the swarm as a whole is being bundled across country by the wind[5,11–16].

That this resultantly downwind mode of 'straightened-out' travel can be adaptive was demonstrated by Rainey[16] in an outstanding example of the application of modern synoptic meteorology to insect ecology. The rainfall desert locusts need for breeding occurs in different regions at different seasons, and results from the temporary convergence of winds upon each region, so that the wind-borne swarms always tend to be delivered to the right place at the right time. Thus a more or less regular seasonal to-and-fro pattern of migrations between geographically discrete regions, on the familiar vertebrate model, and by large powerful insects, can be created not by self-directed flights but by 'passive' displacements. It may still be true that the long-range to-and-fro migrations of some butterflies do not depend on such displacement and are actively oriented, but the onus now lies on students of butterflies to prove it.

That the long-range movements of winged aphids are effected by passive transport on the upper air has been very thoroughly confirmed (mainly with the black bean aphid, *Aphis fabae* Scop.)[17,18]. But their embarkment on, remaining in and disembarkment from this transporting vehicle all depend on active locomotor responses[19]. Embarkment depends on a sharp rise in locomotor excitability in the fresh adult which is triggered into flight, and then directed up out of the vegetation into the free-circulating air, by the bright, predominantly short wave-length light from the sky. This oriented 'straightening out' of its movement does not take the aphid far, but again the direct result is a passive, long-range straightening out of its movement by the fast-moving upper air. Disembarkment depends on a change in the reaction to light as flight proceeds, with a weakening of the kinetic effect and of the attraction to sky light and a relative strengthening of the attraction to the longer wave-length light reflected from plants. Before the phototaxis reverses lastingly to negative, there are intermediate phases when the insects fly about actively near the ground, orienting into and making headway against gentle air-currents and avoiding obstacles, like locusts, and eventually making the alightments by which the flora is sampled for suitable host plants. The intensely active nature of the migratory flight is obvious even in this phase, for the great majority of alighters, even on their own host plants, take off again within minutes.

There is, in fact, a definite inhibition in the young adult of the usual settling, feeding and larvi-position responses to visual and other stimuli from plants, together with an arrest of embryo growth in the ovaries. When the inhibition is eventually removed, by locomotion, embryo growth restarts and at the same time the flight muscles degenerate and the fat body enlarges[19,20]. The restriction of the frenetic migratory activity of these aphids to, at most, a few days and usually a few hours out of the individual's otherwise sedentary life, further underlines the differentiation of migration as a biological function.

What all this means, as Johnson justly insists, is that migration is part of the normal development of winged aphids, "an evolved adaptation"[1]. It is not their reaction to crowding, food shortage or other current adversity as Elton[6], for example, supposed most migrations to be. Nevertheless, although obligate in the winged form of aphid, migration is facultative for the species. Production of the winged form is the response of the wingless form to crowding and other signals of impending adversity. With locusts, too, migration of the persistent lifelong type seen in the gregarious members of swarms is not obligatory but facultative for the species and results from a heritable response to crowding. Migration is often facultative without obvious polymorphism, as in the pierid butterfly *Ascia monuste* L., where it seems to depend on both population density and the time of day of emergence[21]. If, as Southwood argues, migration is usually an adaptation to a temporary habitat[22], then whether it is obligate or facultative may depend on whether the habitat typically lasts long enough for only one generation or for more.

Proposed Non-behavioural Definitions of Migration

Rainey[13] claims with justification that recent work on locusts has "dispelled some of the mystery" in Williams's picture of migration. The mystery was primarily behavioural, and in dispelling it neither Rainey nor Johnson puts anything in its place so far as behaviour is concerned, rather shifting the emphasis to some other aspect of migration. Thus Rainey insists that the effects of vertical and horizontal air-currents on insect displacement must be assessed before the "finer effects" of behaviour, "in order to distinguish what the organism is itself doing from what is being done to it by the environment"[13,16]. But Rainey has himself reported that the members of small swarms do not allow themselves to be dispersed upwards, like aphids, by turbulent convection, when the members of large swarms do[15]. This is but one illustration of the need to assess what both the insect and the environment are doing, simultaneously. Rainey suggests that migration is "more usefully characterized by a seasonal displacement of populations than by directionally purposeful behaviour"[5]. The qualification "seasonal" is not generally applicable since aphids and other insects often migrate in response

to irregularly arising local conditions. It is not necessary to fall back on a purely ecological description like "population displacement", for "directionally purposeful behaviour" is no longer the only alternative.

Johnson recommends distinguishing migration flights "chronologically in the first place before attempting to distinguish them behaviourally"[1]. Disregarding migration other than by flight, he adduces evidence that migratory flights usually occur as the first flights of new adults. There are a good many exceptions to this post-teneral rule, notably post-diapause migrations[4]. But most of them, although not all, would be covered if migration in adult insects were characterized as pre-reproductive, rather than post-teneral. This is an important new common feature recognized in migration: a pointer to developmental physiology (below). Nevertheless, it is as new adults that insects first fly anyway, so the timing does not distinguish migration. The timing of an event becomes of interest once we know what the event is.

Johnson gives two reasons for believing there is no satisfactory way of characterizing migration behaviourally[1]. He doubts whether there need be any difference of kind between migratory and other flights, and earlier questioned the validity of Berland's division of the atmosphere into "terrestrial" and "plankton" zones for flying insects[17]. But that general idea has now been revived in Taylor's concept of a "boundary layer"[18]; and Johnson[1] concedes there is a clear difference between migratory and other flights in Lepidoptera and mosquitoes. The difference is equally apparent in locusts[19,20] and aphids[19] and other insects[20]. His second and more important reason for omitting behaviour from his general system is that the behavioural qualities of migrants "are so variable that definitions based on them as to what is or is not 'migration' or what is 'active' migration and what is 'passive' dispersal become arbitrary, controversial and unsatisfactory when applied to all the types of insect that are said to migrate"[1]. It is true that those distinctions have now broken down, because they assumed a single mechanism of "straightening out" of movements, when as we have seen there are two, discussed further below. At the level of reactions to particular stimuli there is great variation; but the resultant straightening out remains a common feature.

Without that straightening out (the "klino-kinetic" component) even very persistent locomotor activity is not migration, for example in a stationary swarm of flying midges. But when combined with it, a second common feature is what Andrewartha and Birch[9] give as the main one: a special readiness to move (the "ortho-kinetic" component). Here again various stimuli and reactions may be involved. Persistent employment of the insect's own locomotor organs is most common; but there may be no more locomotion than that involved in leaving the feeding or hibernation site and releasing the foothold or clambering on the body of a winged migrant[22,24]. But again, a common feature remains in the special readiness to move and go on moving.

Negative Features of Migratory Behaviour

If we consider only those reactions that show heightened excitability (low threshold) in migrants, we cannot make any all-embracing generalization about them except in terms of their resultant effect: straightened-out movement. That common behavioural feature is important; but it does not entirely dispose of Johnson's difficulty, for it does not provide a ready means of distinguishing migration from such long unidirectional movements as those of an ant toward the nest, a chafer toward a clump of trees, a mosquito toward a host, or a male moth toward a female[25]. But a further criterion is available in what the migrant does not do.

In a migrant the persistently lowered threshold of responses resulting in straightened-out movement goes with a persistently raised threshold of responses that arrest and deviate movement. With locusts and aphids in mind, these more-or-less inhibited reflexes have been generalized as "vegetative", for lack of a better term, meaning responses promoting growth, of the larva or of the adult's genital products, through the exploitation of present resources[26]. The locomotor ones among them were called "station-keeping" responses. Migrants are distinguished by "a transient accentuation of locomotor functions with depression of vegetative functions, such that the insect now travels, by what method being a secondary matter"[19]. Nielsen and Nielsen[21], Blunck[27] and Provost[28] directed attention to this unresponsiveness in migrant butterflies and mosquitoes, and Andrewartha and Birch[9] made the same general point. Thus the Nielsens listed the reflex patterns of adult *Ascia monuste* "living in a territory" as feeding, mating, egg-laying, basking and cleaning, and reported failure to respond to the appropriate stimuli for any of these when the butterflies were engaged in unidirectional flight elsewhere.

The relative degree to which the diverse "vegetative" reflexes are inhibited varies greatly. But the grouping of them under one label is no mere descriptive convenience. In the aphid they are allied reflexes in the physiological sense, standing together in antagonistic relationship to locomotion[29]. This is so when the insect is not migrating also. But then the vegetative reflexes are readily excitable and only briefly inhibited centrally by a stimulus that provokes locomotion instead. When migration starts they are deeply and lastingly inhibited. A more complete characterization of migratory behaviour is then: persistent, straightened-out movement that is accompanied by and dependent upon the maintenance of an internal inhibition of those "vegetative" reflexes that will, eventually, arrest movement. Conversely, the locomotor reflexes (or other reflexes securing displacement) cannot for some while be inhibited by stimuli that do promptly inhibit them at other times.

The distance moved is indicative but not always a reliable criterion of migration, as Provost[28] and Andrewartha and Birch[9] point out, because an insect that is ready to respond to an arresting stimulus may not receive it for some time. Hunting and foraging movements may be very extensive, as in some mosquitoes, yet not be migration if the insects stop as soon as feeding stimuli are received. On the other hand, when an army ant colony, on the emergence of a new brood of worker adults, enters on a 'nomadic phase' in which the workers shift the larvæ to a new bivouac site every night along one of the trails they used for foraging that day, this is migration[30]. In the laboratory, starvation produces a high level of locomotor activity in

blowflies; but this is not migration physiologically speaking, since the flies take sugar as soon as it is presented and as a result of filling their crops with it become lastingly less active[21]. On the other hand, when locust 'hoppers' or Mormon crickets[22] launch into 'marching' and are stopped only temporarily by suitable food plants, this is migration when compared with the behaviour of the solitary individuals. Young adult dragonflies which disperse in all directions away from the edge of the water in which they developed may also be showing an elementary form of migratory behaviour, because at this time they are positively repelled by the sight of water which will later attract them[23]. Teneral adult *Calliphora* will burrow for hours while they remain in soil, but this is not migration, for emergence from the soil at any time stops the movement[24]. On the other hand, the adult female of *Anopheles sacharovi* may truly migrate when it enters diapause in the autumn, for, unlike the non-diapausing female of previous generations, its flying is apparently not arrested by the first blood meal and shelter it finds, so that it travels far from the breeding place[25].

Thus there is an objective experimental method of deciding whether a moving insect is migrating or not, by measuring its responsiveness to the stimuli signalling the appropriate 'vegetative' requirement. This test has seldom been applied, so that it is often impossible to draw any firm conclusion from the literature. When the insects are known to travel on the upper air the tendency is to assume this is mere 'vagrancy': an 'involuntary' consequence of non-migratory behaviour under special conditions (Williams's "overpowering forces"). The spruce budworm (*Choristoneura fumiferana*) is a good case in point, for it has been studied extensively[24]. Much is known about the immediate triggering stimuli for flight and the air conditions favouring transport, but little about changes in the responsiveness of the individuals. It appears, however, that both larval and adult dispersal are increased actively when the population rises to very damaging densities. The reduced fecundity of the resulting undersized adults is partially compensated by their readiness to fly upwards and thus be transported to undamaged trees before depositing any eggs. The larger, more fecund females produced at less-damaging densities do not fly at all until after they have deposited one or two egg masses[24]. But whether there is any difference of kind between flights before and after oviposition, and whether there is a temporary internal inhibition of oviposition in the undersized females, are still unexplored questions.

The idea of temporary inhibition of 'vegetative' responses in migrants has often been conveyed in a subjective, teleological way that confuses means with ends and serves as a substitute for, rather than an invitation to, experiment. Migratory behaviour has been distinguished as not searching (for any vegetative requirement: food, mate, oviposition site, etc.), not internally oriented, non-motivated, non-appetitive[9,21,26]. The inference is that any movement with a specifiable end is not migratory (see Provost[26] on pre-hibernation flights of anophelines). But migratory and non-migratory movements both end with readiness to respond to some specific stimulus signalling a vegetative requirement or resting place, and in neither case is the movement directed by its end. In both, the locomotion is, in fact, centrally antagonistic to the reflexes that terminate it, at first inhibiting them and finally being inhibited by them in turn. The only objective sense in which a movement is directed toward an end is that the antagonistic arresting reflexes may be progressively 'primed' (thresholds lowered) as a result of being inhibited by the locomotion (successive induction[29]). The basic difference between migratory and non-migratory behaviour is a difference of relative thresholds. There is no sharp line of demarcation between them; we are concerned rather with degrees of functional differentiation in a particular direction, and our first concern is to identify that direction.

Physiological Differentiation in Migrants

The study of insect migration will remain in its present backward state until we know more of the sensory, nervous, endocrine and metabolic components of the mechanism by which migration is 'primed' (in addition to the immediate stimuli that elicit the primed responses) and likewise of the reverse changes that follow on migratory activity. The best information of this kind concerns aphids[20]; but generally there is little. Something is known about fat deposition in place of egg development in migrants[4] as in diapausing insects, about flight muscle development in place of eggs[26] and the use of fat as the most economical flight fuel for migrants[27].

Ecologically, migration sometimes looks like an alternative to diapause when conditions will no longer permit growth, development or reproduction[9,22]. It is so when the habitat deterioration is merely local so that vegetative activities can be resumed earlier elsewhere than *in situ*. It is not so when the deterioration is synchronized throughout the insect's range, as in a temperate autumn or dry tropical summer. Migration may then be, on the contrary, a condition for diapause, if that is also not possible *in situ*[4,22]. But physiologically, the important point is that migration is in either case at the expense of vegetative functions in the individual. The internal inhibition of certain reflexes is the behavioural component of a whole physiological syndrome.

Fig. 1 illustrates this by comparing the timing and amount of growth or reproduction in migratory and non-migratory (or less migratory) females of the same species in the laboratory, where actual migratory activity is minimal and vegetative requirements are continuously available. Solitary locusts (Fig. 1, right) migrate as young adults between seasonal habitats, but the syndrome is developed to an extreme in gregarious locusts which migrate throughout their lives and will not settle in any place[23,26]. Gregarious locusts may show hastened instead of retarded oviposition when there is a tendency to diapause governed by length of day, but in either case they lay considerably fewer eggs[11,12]. The garden chafer (*Phyllopertha horticola* (L.)) is another interesting variant[13]. All the females are ready to lay on emergence before any flight, and most lay their eggs then and do not migrate. The migrants are females that did not lay the bulk of their eggs on emergence and thereafter seem to have developed an inhibition of the reflexes associated with laying; they lay readily after migrating.

The nature of the physiological syndrome in migrants—accentuation of 'sensori-motor' functions with depression of vegetative ones—makes it easier

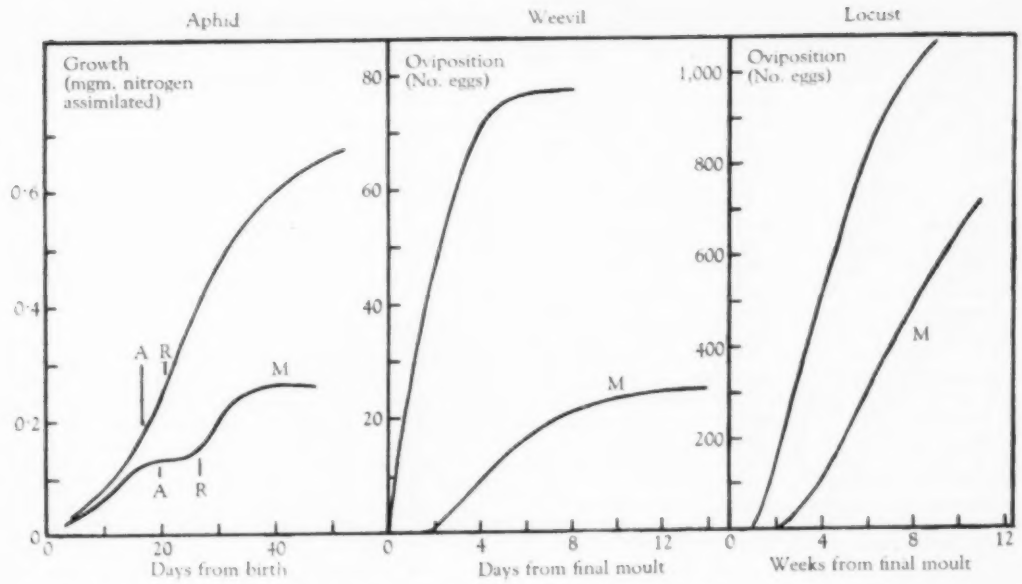


Fig. 1. Examples of the arrest and depression of growth functions in adult migrants (*M* curves). Left: *Tuberolachnus salignus* winged (*M*) compared with wingless form, after Mittler (ref. 38). *A*, final moult to adult; *R*, start of reproduction (larvi-position) after which the further rise represents embryo growth; Centre: *Callosobruchus maculatus* 'active' (*M*) compared with normal form (terminology of Caswell (ref. 39)), after Utida (ref. 40); Right: *Locusta migratoria migratorioides* gregarious (*M*) compared with solitary form, after Norris (ref. 41). All curves cumulative

to understand why migration so commonly occurs in the adult stage and is then usually pre-reproductive[3] or inter-reproductive. For reproduction involves a resumption of the growth functions typical of juveniles, and "an individual is at its most adult during that period of physiological reversal wherein the products of one growth phase are not added to but employed and consumed in ensuring the success of the next"[36]. In this sense migration is physiologically 'super-adult'. In that light it is equally understandable that the next most common stage at which migration differentiates is the first instar larva. This stage is better fitted than later larval instars, because it often has to travel farther than them at any rate when the eggs are not laid directly on the food, it is smaller and hence more buoyant, and more numerous.

At the same time the negative features of migration represent a differentiation in the direction of diapause. Diapause cannot be characterized by one physiological process in all insects. The one common feature is temporary failure to respond by further growth or development to the conditions that will, eventually, promote those processes[14]. Considered physiologically, migration is an example of this rather than an alternative to it.

During the depression of vegetative functions in both migration and diapause some other process occurs which is a pre-condition for their resumption. In diapause this unidentified other process is called "diapause development"[41]. In the winged aphid the equivalent of diapause development is promoted by an antagonistic process, locomotion, which restarts the arrested vegetative functions by central nervous induction[29]. This distinguishes a *locomotory* type of developmental arrest from other types, such as arrests of larval development that are broken by feeding, arrests of egg development or oviposition broken by copulation, and diapauses proper in which the nature of the response promoting diapause development is still unknown, but the stimuli are known to be low temperature or photoperiod[44]. By no means all the developmental arrests in migrants can be assumed to resemble the aphid's, for some are typical extended diapauses covering also periods of complete inactivity[4]. But in the common situation where the developmental arrest ends with the travelling, it is suggested as a working hypothesis that the two are causally related as in the aphid.

It follows from all this that when, as frequently happens, a deterioration in individual size, fecundity or other vegetative properties is observed under certain conditions, this should not be taken as wholly negative in effect until the possibility of an accompanying increase in migratory capacity has been excluded.

Ecological Functions of Straightened-out Movement

Resultantly downwind displacement independently of orientation was not recognized as a migratory "straightening-out" mechanism by Williams. But it also brings about long-distance travel, instead of confinement within a small area through frequent changes of direction, and does so on a larger scale than does oriented movement on or near the ground; and it results from the active, specialized behaviour of the insects. In locusts, aphids and many other insects[1,22] this consists in rising actively away from the ground and so out of what Taylor[18] calls the "boundary layer" within which non-migrants actively confine their movements. Such resultantly downwind travel cannot therefore be dismissed as the "passive distribution of individuals by overpowering

forces", which Williams[2] excluded from migration. It can be assimilated readily into his definitions of migration cited in the first section above, provided we do not read into them his restrictions.

Moreover, these two mechanisms of straightening out, actively oriented and passively wind-borne, can be observed at different times in the same migrant, powerful locust and weak aphid alike. Migrants cannot therefore be separated into two classes according to which mechanism they exhibit, although they may differ in the relative importance of the two mechanisms in their migration. After their oriented ascent, aphids use the wind-borne mechanism in the earlier part and the low oriented one toward the end of a migration[19]. Garden chafer migrants seem to use the two more equally from the start[42]. According to the available accounts[2-4,21], many butterfly migrants keep close to the ground more persistently than aphids, chafers or locusts, and may thus use the oriented mechanism during a greater proportion of their time, although this does not necessarily mean for the greater part of the distance they travel.

Hitherto, it has been solely in the context of seasonal to-and-fro migrations between geographically discrete regions that the ecological function of straightening out seems to have been considered. Williams's hypothesis that straightening out is directionally adaptive, serving to direct the migrants to the right place at the right time, provided the motive for his successful search for evidence of return movements; and his hypothesis has now been confirmed for the seasonal movements of locusts by Rainey[16]. But the continued migratory movements of locust swarms through the mosaic of soils and vegetation within a wind convergence zone where suitable food plants and oviposition sites occur in patches are not directionally adaptive. Some long-range seasonal movements of aphids and other small plant-feeding insects seem to deliver them also to suitable breeding areas[43]. But again this is not true of their movements within very considerable regions wherein the host plant is not concentrated in one place but patchily distributed. Many sorts of habitat, hibernation site, etc., are similarly scattered.

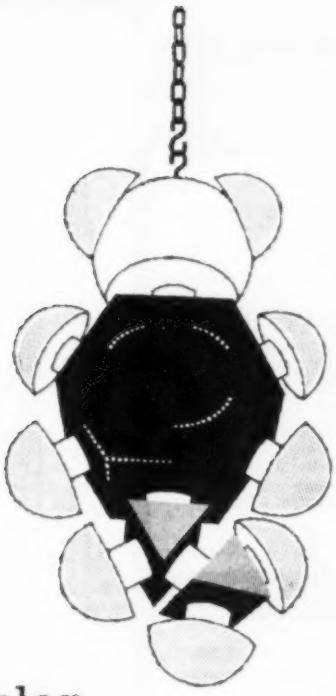
In that situation migrants are no more likely to find what they require in one direction than in any other, or at one distance more than another. The straightening out of their movements has then no directionally adaptive significance. They travel in many directions by both straightening-out mechanisms; and this is adaptive inasmuch as some of them find the requirements in all directions and at all distances. Given enough individuals, the two mechanisms together make an efficient 'scanning' device that works on a coarse and a fine scale by means of long wind-borne, and short, low-level, oriented traverses, respectively.

Straightening out here serves the simpler and, presumably, more primitive function of displacement *per se*: the opposite of 'station keeping'. This is not, of course, an efficient procedure so far as the individual is concerned. The positive advantage of having large numbers of individuals if the migratory habit is to develop[19,26] is a point that has been little considered in discussions of the association between density and migration. Enormous losses of individuals *en route* certainly occur, and even entirely abortive movements by enormous numbers of individuals together, as in Elton's famous case of the lachnids on Spitsbergen. But these losses the species can evidently afford; and if migration tends to be associated with temporary habitats[22] this may mean that such habitats tend to permit higher multiplication-rates than permanent ones. The losses do not call in question the adaptive value of the behaviour pattern that brings them about because the same behaviour brings about biologically successful movements as well, with the added advantages of escape from overcrowding, enemies, etc. What the procedure does achieve is a very efficient coverage of the available habitats over a large area and avoidance of 'too many eggs in one basket'[19].

Given multi-directional movements between places arranged in mosaic the evolutionary problem of return movements disappears, as Wiltshire[38] pointed out in connexion with butterfly migrations. Many species of aphid alternate seasonally between woody and herbaceous plants. It has never been supposed that the descendants of a given individual necessarily returned to the same tree the same year. Nevertheless, untidy, constantly reshuffled returns are assumed, and no problem has been raised of how the migratory habit could persist in the population. The same applies to any insects that repeatedly disperse and colonize new habitats available at the time, new or old, so that no particular movement can be singled out as a return.

Movements of this kind are so common as to be of most interest to ecologists, but are included under dispersal rather than migration[9] because they are not directionally adaptive. Since that is a secondary matter it seems best to apply the term migration, as Johnson[1] and Southwood[22] are now in effect doing, to all cases where a change of location can be shown to be an active 'evolved adaptation' along the lines distinguished here, regardless of exactly how or at what stage in the life-history it occurs. The continued use of dispersal instead of migration for the particular mechanism of transport by wind or water can cause only confusion. Dispersal will, no doubt, continue to be used in the purely spatial sense of population scattering, especially when a loose term is needed because there is not yet enough information to judge whether the movement is migratory or not. If it is used in any more precise sense this should be specified. Thus dispersal is likely to be used for non-migratory movements involving no general inhibition of vegetative reflexes, but merely a change in them, as when the adult's food is different from the larva's; or for movements that may involve some temporary inhibition of them, as when new-hatched caterpillars scatter over a uniformly palatable leaf, but are not persistent or straightened out enough to rate as migration.

To sum up: recent work has undermined C. B. Williams's behavioural assumptions about insect migration while confirming his idea that it is a differentiated biological process. Migration is a persistent, straightened-out movement with some internal inhibition of the responses that will eventually arrest it. It may be effected by the insect's own locomotory exertions or by its active embarkment on some transporting vehicle. These are the behavioural aspects of a physiological syndrome which is 'super-adult' in character but may develop at any stage of the life-history, and in common with diapause involves a phase of depression of 'vegetative' (growth-



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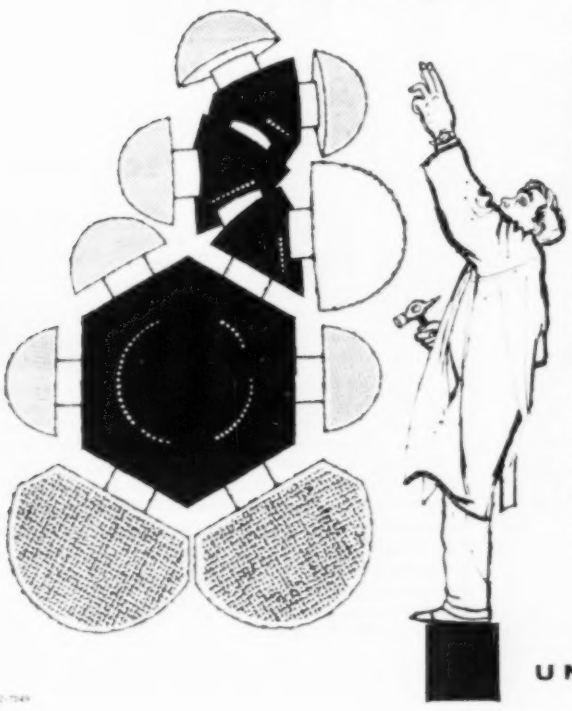

It is always interesting to study a natural organic compound, to note the ingenuity and specificity of its synthesis, and its ultimate fitness for purpose. Scientists cannot yet match nature in the specificity of her methods, but they can do so in ingenuity and occasionally excel her in fitness.

Take organic fluorescers, for example, of which many man-made varieties are better than the best natural product. Herschel, Brewster and Stokes, in their original work on fluorescence, used quinine sulphate. They were interested in the physical phenomenon. Knorr, a chemist, was more interested in the pharmacological action of quinine, and his studies of related heterocyclic nitrogen compounds led to the syntheses of the pyrazole and pyrazoline five-membered rings.

In so doing he paved the way also for more active fluorescers. Bowen has pointed to the importance of electron donors and acceptors in fluorescence, and the need for a conjugated system of Pi electrons only lightly coupled to the molecular lattice to limit the dissipation of resonant energy. Both he and Pringsheim have discussed heterocyclic compounds in this context and shown that rigid molecular structure and internal conjugation are conducive to fluorescence.

Pyrazole itself does not provide a suitable nucleus since the carbon-carbon double bond acts as an electron trap in the heterocyclic ring system, but diaryl pyrazolines are excellent fluorescers, and Kendall and Duffin, and Neunhoeffer and Rosahl, have made broad studies of the group. Unilever are active in the study of these fluorescers, and Chase and co-workers have made a close study of the relation between structure and fluorescent characteristics.

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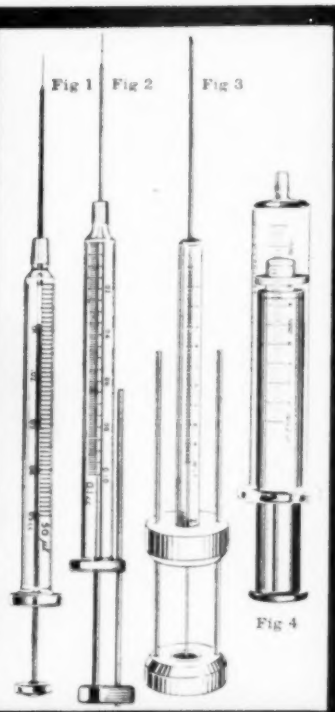

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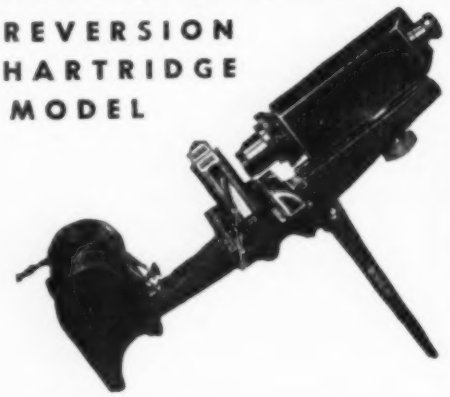

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promoting) functions as a condition for their resumption.

Grateful acknowledgment is made to Drs. A. D. Lees, P. E. Madge, T. R. E. Southwood and B. P. Uvarov, and to Prof. V. B. Wigglesworth, for their criticisms of this article in draft.

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FLUCTUATIONS IN EQUATORIAL STRATOSPHERIC WINDS

By R. A. EBDON and R. G. VERYARD

Meteorological Office, Air Ministry, Harrow, Middlesex

THE predominance and persistence of easterly winds, especially above the level of the tropopause, is a well-known feature of the airflow over equatorial regions. This could be attributed to an inflow of air towards the equator; air moving towards the equator tends to retain the angular momentum about the Earth's axis which it possesses as a result of the Earth's rotation, and it therefore tends to arrive at the equator as an easterly wind. But westerly winds, that is, air moving faster than the equator, can also be produced over equatorial regions if there is a pressure gradient along the equator. However, as the net pressure gradient around the equator must be zero, a predominance of westerly winds is not to be expected; indeed, a westerly airflow encircling the equator is very difficult to explain. That there are, in fact, westerly air-streams at certain levels over some equatorial regions has been known for some time.

There are, for example, the large-scale westerlies in the lower troposphere associated with the flow patterns of the monsoons; but these are not surprising because of the substantial pressure gradients in the monsoon regions. But an explanation in terms of the pressure pattern of the occurrence of quasi-permanent westerlies in the equatorial stratosphere, sometimes called the 'Berson' westerlies (because it was A. Berson who first directed attention to the existence at about 20 km. of a narrow belt of westerly winds in the lower stratosphere over central Africa), has not proved practicable.

Moreover, it has been alleged by some workers that the Berson westerlies constitute a narrow ribbon of west winds extending right round the equator, and, as indicated above, this presents a challenge to dynamical meteorology. However, the idea which has been given in many meteorological publications, that the equatorial stratospheric westerlies occur with a regularity and persistence comparable to that of the equatorial tropospheric easterlies, needs some modification. Indeed, it would appear that in the lower equatorial stratosphere the zonal component of the wind, that is, both the easterlies and the westerlies, is subject to marked fluctuations—one regime replacing the other at intervals of a year or more[1–3]. Not only do data (based on radar wind ascents reaching 50 mb. and above) indicate that, for some months, there can be very considerable variations in the equatorial stratospheric winds between one year and the next, but they also show that westerly winds can occur not merely in a shallow layer but also throughout the

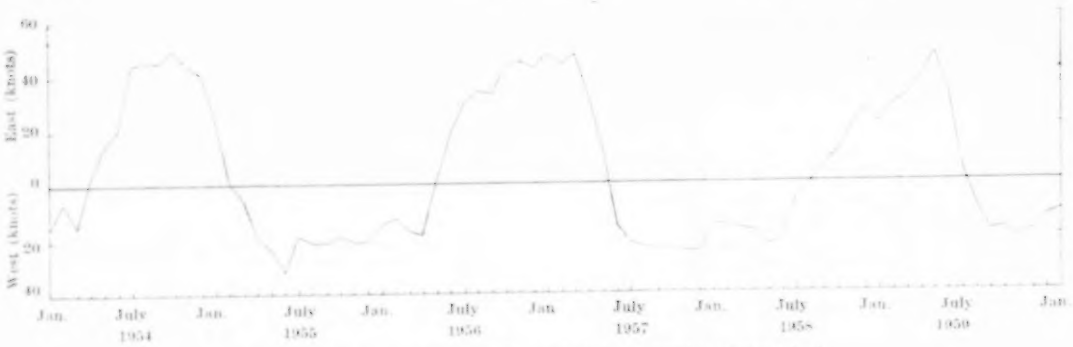

Fig. 1. Monthly mean values of 50-mb. zonal wind component at Canton Island

lower stratosphere from the tropopause upwards to above 30 mb.

The monthly mean values of the zonal wind components at 50 mb. for Canton Island (02° 46′ S., 171° 43′ W.) for the period January 1954–February 1960 are shown in Fig. 1. It will be seen that there is a fluctuation with a period of about 25–27 months. Although only a few years data are available for analysis, this fluctuation is also evident in Fig. 2, which gives a curve of the monthly mean values of the zonal wind component at 60 mb. at Nairobi (01° 18′ S., 36° 45′ E.) and in Fig. 3 giving similar curves at 30, 40, 50 and 60 mb. for Christmas Island (02° 00′ N., 157° 23′ W.). At these stratospheric levels the wind direction at the stations considered is nearly always either almost due easterly or almost due westerly, except during the months when the change-over from one regime to another occurs. Once a predominantly easterly or westerly flow is established it tends to persist for some 10–13 months, although in any one month there may be a few days when the direction is reversed. The in-phase agreement between the 60-mb. curves for Nairobi and Christmas Island is quite remarkable. Similar results have been obtained for the zonal winds at 60,000 ft. (about 65 mb.) for the period 1954–60 at Singapore (01° 20′ N., 103° 53′ E.); and shorter period data for the 50-mb. level at Recife (08° S., 35° 53′ W.) show that the phenomenon also occurs at that station. Indeed, the evidence suggests that the fluctuation occurs more or less simultaneously at the same level all round the equator. In any event, the results indicate that, in the equatorial belt, a mean monthly (or yearly) wind obtained by averaging over a period of years will be very misleading if regarded as representative of the average wind in any particular month (or year), as is commonly done in climatology.

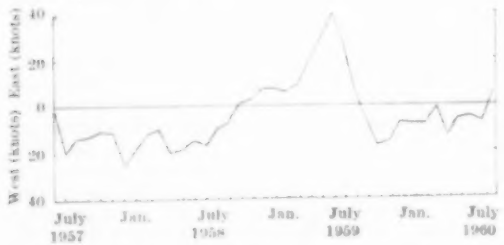

Fig. 2. Monthly mean values of 60-mb. zonal wind component at Nairobi

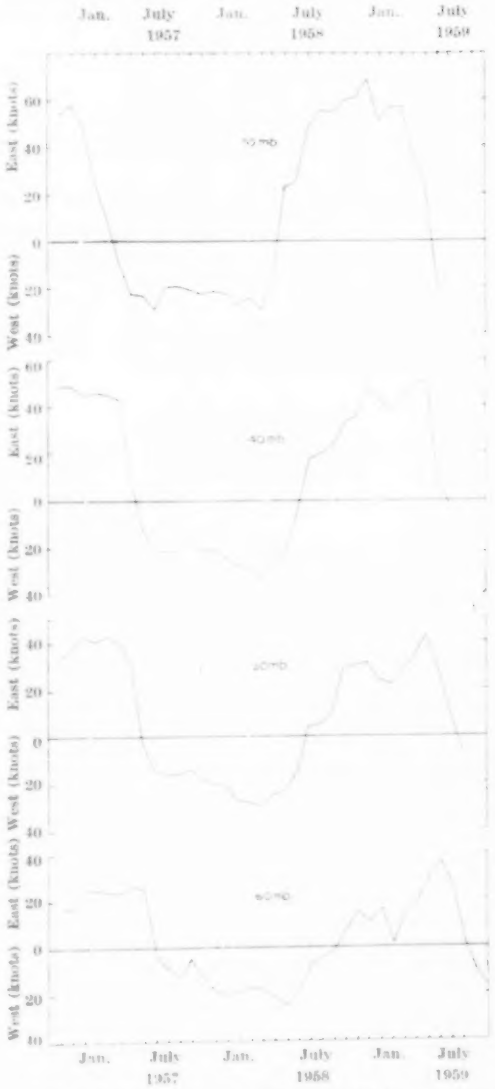

Fig. 3. Monthly mean values of zonal wind component at Christmas Island at 30 mb., 40 mb., 50 mb. and 60 mb.

Table 1. Months during which the Mean Zonal Wind Component at Christmas Island changed sign

Level	From east to west	From west to east	From east to west
10 mb.		(Oct. 1957)–(Nov. 1957)	
20 mb.	Oct. 1956–Nov. 1956	(Dec. 1957)–(Jan. 1958)	
25 mb.	Dec. 1956–Jan. 1957	Mar. 1958–Apr. 1958	Apr. 1959–May 1959
30 mb.	Feb. 1957–Mar. 1957	Apr. 1958–May 1958	May 1959–June 1959
40 mb.	Apr. 1957–May 1957	June 1958–July 1958	June 1959–July 1959
50 mb.	Apr. 1957–May 1957	June 1958–July 1958	July 1959–Aug. 1959
60 mb.	May 1957–June 1957	Sept. 1958–Oct. 1958	Aug. 1959–Sept. 1959

Table 1 shows the months during which the mean zonal wind component at levels above 60 mb. at Christmas Island changed from easterly to westerly or vice versa. (The two bracketed entries are based on the maximum winds reported, as insufficient data were available to give monthly mean values.) It will be seen that, as was found by Viezee[2], the change in wind direction occurs first in the higher stratosphere and then gradually descends. The one occasion when it was possible to detect the change at 10 mb. suggests that it takes almost a year before the change in wind direction at 10 mb. reaches 60 mb. When the change in wind direction occurs at 25 mb. it is some 6 months later before the corresponding change occurs at 60 mb. The curves in Fig. 2 show that the amplitude of the fluctuation decreases downwards.

From such investigations as have been possible with the data available there was no detectable connexion between these events in the equatorial stratosphere and events in the equatorial troposphere. If adequate data are available, it is hoped to determine the extent to which the fluctuation extends north and south of the equator. Results so far obtained suggest that within 10° the fluctuation still exists but with decreased amplitude.

This communication is published by permission of the Director General of the Meteorological Office, and the subject is discussed in detail in a paper which will be published elsewhere.

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NEWS and VIEWS

Mineralogy and Petrology at Cambridge : Prof. C. E. Tilley, F.R.S.

Prof. C. E. Tilley is retiring from the professorship of mineralogy and petrology in the University of Cambridge at the end of the present academical year. On the retirement of Prof. Hutchinson and of Dr. Harker in 1931, the professorship of mineralogy and the readership in petrology were combined in a new chair of mineralogy and petrology, of which Prof. Tilley was the first holder. During his tenure of thirty years he has not only been exceptionally active in research, but also has been the leader in building a department of world-wide influence in its field. In addition to teaching and research in mineralogy and petrology, the Department has contributed much to the teaching of crystallography and to the crystallographic study of minerals. Prof. Tilley has played a full part in university life, having served on the Board of Research Studies, the General Board and the Council of the Senate. He was also for many years chairman of the Faculty Board of Physics and Chemistry, and was vice-master of Emmanuel College from 1952 until 1958.

Prof. W. A. Deer

Prof. W. A. Deer, who has been appointed to succeed Prof. Tilley, has held the chair of geology in the University of Manchester for eleven years. He has brought into existence there a thriving research school, the distinctive feature of which is the application of modern physico-chemical techniques to the solution of geological problems. In 1953, together with Prof. L. R. Wager, of the University of Oxford, he led a geological expedition to East Greenland, continuing investigations which had been interrupted by the Second World War. He has since directed various mineralogical researches on the rocks of the Cape Edvard Holm area, most of them still unpublished, but all of the high standard that has always characterized his work. Of recent years, he has spent much time writing a new book on rock-forming minerals in association with two members of the Manchester staff, Dr. R. A. Howie and Dr. J. Zussman. Active as he has been in geological work, Prof. Deer has found time to play an ever-increasing part in general university affairs. He has been chairman of the Executive Committee of the General Board of Faculties, and of the Science and Technology Section, and has served on committees too numerous to mention here. Particular reference should, however, be made to his work in the implementation of the extensive building programme on which the University of Manchester is now engaged.

British Drop Forging Research Association : Mr. P. H. R. Lane

Mr. P. H. R. Lane, head of the Members' Service Department of the British Welding Research Association, has been appointed the first director of research of the Drop Forging Research Association. Mr. Lane was educated at Alleyn's School, Dulwich, and Strand School, Elm Park. He obtained an honours degree in metallurgy at the University of London and afterwards joined the staff of the British Welding Research Association. He was first engaged in metallurgical work on the weldability of low-alloy high-tensile steels. In 1950, he transferred to the engineering section to work on the design of pressure vessels and pipe-line components, and for five years was in charge of the department dealing with this work. During this period he was also associated with work on the brittle fracture of steel plates and on the fatigue strength of welded components. In 1957, he returned to metallurgical work as deputy chief metallurgist of the Association, in charge of all ferrous metallurgical investigations. In 1959, he was appointed to the new position of head of the Members' Service Department, which is responsible for all contacts with the

members of the Association. Mr. Lane is an associate of the Institution of Metallurgists, and an associate member of the Institute of Welding. He has published many papers on both the metallurgical and engineering aspects of welded fabrications and also on the techniques of experimental stress analysis.

The Mellon Institute : Research Directors

Drs. A. A. Bothner-By, Thomas G. Fox and Harold P. Klug have been appointed research directors in the Mellon Institute, Pittsburgh. Dr. Bothner-By joined the Institute in 1958 as a Staff Fellow and has been an assistant director of research since 1959. He is recognized as an authority on the use of nuclear magnetic resonance in organic chemistry, and has developed a centre of research in the latter field at the Institute. Dr. Fox joined the Mellon Institute in 1957 as an assistant director of research and has headed a large part of the Institute's extensive polymer research programme. He is known for his work in the chemistry and physics of rubber and other polymers. Dr. Klug joined the Institute in 1945 as an Administrative Fellow after eighteen years as a professor of chemistry in various universities. He became an assistant director of research in 1959. A specialist in structural physical chemistry, Dr. Klug is the author of two books and numerous papers.

Cultural Contacts in the British Commonwealth

Replying to questions in the House of Commons on March 2, Mr. D. Sandys, Secretary of State for Commonwealth Relations, said that the Government wishes to encourage the development of closer links between young people in the Commonwealth, and, besides initiating a programme for providing 5,000 additional places for overseas students in hostels where they will live and mix with British students, it proposes also to provide a number of new or enlarged social and cultural centres to be run by the British Council. The Government is prepared to meet the capital expenditure involved up to a maximum of £3 million, and will, as at present, consider applications for financial assistance to voluntary bodies concerned with Commonwealth youth. It is hoped, however, that private support will also be forthcoming for such projects and that the voluntary organizations active in this field would bear some share of the cost. Mr. Sandys expressed the Government's appreciation of the work of Field Marshal Sir Gerald Templer's Committee on this question. He said that the Government would welcome any reciprocal action in this sense among Commonwealth countries, and that the British Council had been authorized to consult voluntary organizations, the universities and other educational authorities and institutions about the whole programme. He undertook to see that the nature of the scheme was made widely known throughout the Commonwealth.

The Dounreay Fast Reactor

In written replies to questions in the House of Commons on February 28 about the Dounreay fast reactor, the Parliamentary Secretary for Science, Mr. D. Freeth, said that the work at Dounreay, though widely diversified, is concerned mainly with developing the fast reactor system. Construction of the fast reactor was completed during 1959 and a series of low-power tests have been completed ; tests in the megawatt range will shortly begin. The reactor will then be gradually worked up to full power. The reactor first went critical in November 1959, and the main problems encountered since have not been concerned with the nuclear side of the experiment. No major change in the level of work at Dounreay is contemplated. Mr. Freeth also said that he hoped to make a statement shortly about a low-power nuclear reactor for the universities and colleges of technology.

Scientific and Technical Personnel in American Industry

A survey of the employment of scientific and technical personnel in private industry in the United States in January 1959 was conducted for the National Science Foundation by the Bureau of Labour Statistics of the Department of Labour as part of a comprehensive programme of studies of scientific and technical personnel in all sectors of the economy (Pp. vi+66. Washington, D.C. : Government Printing Office, 1960. 45 cents). Estimates showed that of 800,000 scientists and engineers employed in American industry in January 1959, 764,000 were employed by the 47,500 firms covered by the survey. Engineers numbered 615,000 or 80 per cent, and the 149,000 scientists included 72,000 chemists, 18,000 biologists, 15,000 physicists and 15,000 geo-scientists. Aircraft, electrical equipment, chemicals and machinery accounted for 45 per cent of the scientists and engineers covered by the survey ; but in the industries covered scientists and engineers represented only about 3 per cent of the employees, varying from 11 per cent in aircraft manufacturing to 0·3 per cent in textiles and apparel. In manufacturing industries, firms with 5,000 or more employees accounted for nearly two-thirds of the scientists and engineers, but only two-fifths of the total labour force. Of the 277,000 scientists and engineers employed in research and development, about 5 per cent were employed in administration ; 235,000 were employed full-time in research and development, the remaining 40,000 being engaged also to a significant extent in other activities. Only in production and operational work were more scientists and engineers employed than in research and development, inspection quality control, or other production and operational work accounting for 39 per cent of the total. Almost 550,000 technicians, or about 72 for every hundred scientists and engineers, were also employed, and of these about 250,000 were classified as engineering and physical science technicians, more than 195,000 as draughtsmen, and 16,000 as medical, agricultural and biological technicians. In research and development about 156,000 technicians were employed, or 56 per 100 scientists or engineers. A comparison with previous surveys indicates that the employment of scientists and engineers grew much less in the years immediately prior to 1959 than in 1954–57, and even in research and development the rate of increase decreased from 13 per cent per annum between 1954 and 1957 to 7 per cent between 1957 and 1959 ; the increase being largest with mathematicians (17 per cent) and smallest for chemists (3 per cent).

Research in Biochemistry and Allied Sciences in Great Britain

At the Cardiff meeting of the British Association for the Advancement of Science in September 1960, a discussion was held, under the joint auspices

of the Biochemical Society and Section I (Physiology and Biochemistry) of the Association, to consider the financing of biochemical research in Britain (see *Nature*, 188, 194; 1960). Because of their wide interest, the Biochemical Society has now published the proceedings of this meeting (*The Organization and Financing of Research in Biochemistry and Allied Sciences in Great Britain*. Edited by K. S. Dodgson. Pp. 51. London: The Biochemical Society, 1960. 2*s*. 6*d*.). Nine speakers were chosen, who were particularly concerned with the organizing and financing of biochemical research in Britain. After an introduction by Prof. A. Haddow, the role of the following organizations was described: Medical Research Council (Dr. F. J. C. Herrald), Agricultural Research Council (Sir William Slater), Department of Scientific and Industrial Research (Mr. C. Jolliffe), and the Imperial Cancer Research Fund (Dr. G. F. Marrian). Prof. F. C. Happold discussed problems of a university department of biochemistry, Dr. F. A. Robinson dealt with biochemical research in industry, and Dr. J. B. Bateman discussed American support of biochemical research in Great Britain. Prof. A. Neuberger summarized the proceedings of the meeting.

The Commonwealth Forestry Bureau, Oxford

THE work of the Commonwealth Forestry Bureau at Oxford has been described and published as an example of the work done by the Commonwealth Agricultural Bureaux, of which it is the youngest member (*A Synopsis of the Work and Growth of the Commonwealth Forestry Bureau, Oxford, 1939-1959*. Pp. 27. Oxford: Commonwealth Forestry Bureau, 1960. 2*s*. 6*d*.). The Bureau was formed in 1939 to serve foresters, wood technologists and scientists in associated fields throughout the Commonwealth, but from the first the quarterly publication, *Forestry Abstracts*, attracted subscriptions from foreign countries, and the Bureau and its periodical are now internationally known; the abstracts reach more than ninety countries. The principal work of the Bureau is the quarterly publication of *Forestry Abstracts*, which notices, by abstract or by title only, more than 5,000 publications annually on forestry and associated subjects.

Medicine and Public Health in China

IN a paper presented at the meeting of the American Association for the Advancement of Science on December 27, Dr. William Y. Chen, U.S. Public Health Service, discussed the condition of medicine and public health in modern China. The main sources of information for the preparation of the paper were various medical and public health journals published both in Chinese and English during the past ten years. The picture is presented against the background of medicine and public health in pre-Communist China, and shows that the most remarkable accomplishment has been the prevention and control of many infectious and parasitic diseases which have ravaged the country for generations. There has also been an improvement in medical education in quantity if not in quality. Other progress in medicine does not seem to correspond with the claims made for it.

Problems in Cybernetics

A VALUABLE new addition to the steadily growing list of translated Russian scientific journals has recently appeared; it is called *Problems in Cybernetics* (Pergamon Press. Pp. x + 314. Russian editor, A. A. Lyapunov), and it is to be published at irregular intervals. The first issue contains a general article by Lyapunov, entitled "Certain General Problems in Cybernetics", which serves to show just what fields of inquiry the Russians include under the term 'cybernetics' at present (for the boundaries are very nebulous). Particular emphasis seems to be placed on automatic computer programming, for the simulation of all types of control process, including those analogous to certain biological processes; on representation of information and its processing, including that in automatic programme-controlled computers; on mechanization of various thought-like processes, as in decision making, recognition, strategy and various 'goal-seeking' operations. It is planned that the journal will contain, in the future, articles dealing with the theory of algorithms and automatic devices, theory of control and problems of production automation, theory of operations and of calculating machines, and with certain applications of the ideas of cybernetics to biology, economics and linguistics. Also, material will be included of a critical, bibliographical and historical nature, being primarily details of the work of the cybernetics seminar held in the University of Moscow. Particular reference is made to this seminar, which has been held since 1955, with a list of titles of papers; these include work on conditioned reflexes primarily. There are also listed titles of papers read at a technical conference held in 1957 which suggest wider fields of interest; especially applications to linguistics, to automatic translation, to coding of chemical formulæ, to speech analysis, to machine-reading, together with many technological aspects of computer design.

The Association of Universities of the British Commonwealth

THE report of the Executive Council of the Association of Universities of the British Commonwealth for the year ended July 31, 1960, records a membership of 103 universities, 17 university colleges and 4 other approved institutions of higher learning (Pp. 30. London: Association of Universities of the British Commonwealth, 1960). The volume of appointments work continued to increase, and, in one way or another, the Association helped with 877 vacant posts and dealt, mainly by correspondence, with 4,782 inquiries; 1,514 applications were received and the universities announced the appointment of 139 of the candidates who applied through the Association; of these 72 were in Australia, 28 in New Zealand and 20 in Hong Kong. Some account is given of the Association's work under the Commonwealth Scholarship and Fellowship Plan, and of its administration of the Frank Knox Memorial fellowships, the Marshall scholarships, the Imperial Relations Trust scholarships and of the Commonwealth University Interchange, as, for example, in connexion with the new scholarship scheme of the Drapers' Company to enable British schoolboys to take their first degrees at certain overseas Commonwealth universities. Some account of the work of the Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom is appended, together with the accounts of the Association, and a note on the financial statement which records total expenditure of £48,089 and income of £52,187.

The Transvaal Museum

At the present time, museums are extending their ancillary services in many directions while still maintaining their essential function of the collection and preservation of objects. It is interesting to note in this connexion that the Transvaal Museum is sponsoring a bat banding project to serve as an aid in the study of these animals (*Bulletin Transvaal Museum*, No. 5. Pp. 8. July 1960). At present the emphasis is on cave bats and species of the genera *Rhinolophus*, *Miniopterus* and *Myotis* are being dealt with, though house bats such as Tadaridae have also been banded. While most of the work is at present concentrated on the Transvaal, banding in Bechuanaland and Natal has also been carried out. Bats have been recaptured over a maximum period of nearly two years and over the longest distance of about 100 miles. Chameleons have been kept in the museum for the purpose of studying behaviour and the flap-necked, dwarf, forest and horned chameleons have been included in this research. Particular attention has been given to a comparison of the aspects of behaviour in related species and genera.

National Museum of Wales

The fifty-third annual report of the National Museum of Wales for the year ended August 1960 records the welcome grant to the Welsh Folk Museum of £10,000 towards the cost of constructing a new car park and ticket office and for widening the approach road to the new entrance (Pp. 78+4 plates. Cardiff: National Museum of Wales, 1960). In the Department of Geology the systematic and stratigraphical fossil collections have been re-housed, and the model of the Penrhyn Slate quarry and collection of miners' lamps transferred to the new Industry Gallery. The artist in the Department of Botany has made models of 23 flowering plants, all of which replace the less attractive dried material previously on show. In the Glanely Gallery, Department of Zoology, the exhibit of birds' nests and eggs has been reorganized and augmented, and casts have been used to replace spirit specimens. In the Department of Archæology notable progress has been made in modernizing the Roman Gallery, and a careful watch has been maintained for chance discoveries. The Department of Industry was officially opened in May 1960, which event naturally culminated a year of preparation. The Department of Art has been much engaged in the work associated with temporary exhibitions. In this short note it is only possible to mention the highlights in the work of this progressive and stimulating museum.

Nomenclature of Human Chromosomes

The rapid growth of knowledge of human chromosomes and their importance in genetics and medicine have led to some confusion about nomenclature in the literature. Consequently a small study group of workers recently met in Denver, Colorado, to formulate an acceptable scheme of nomenclature (*J. Hered.*, 51, 214; 1960). It was agreed to number the chromosomes serially, from 1 to 22, as nearly as possible in descending order of length; that the sex chromosomes should continue to be referred to as *X* and *Y*, and that the 22 autosomes should be classified into 7 groups, distinction between which can readily be made. Within these groups, especially that comprising chromosomes 6 to 12, and including also the *X*-chromosome, identification of the chromosomes is difficult by present criteria, though it is believed that with very favourable preparations all or most of the chromosomes can be identified. Two valuable suggestions emerged from the discussions. One concerned the storage of documentation for reference, perhaps in a central repository; the other referred to the need to preserve cultures for future reference, comparison and exchange.

Studentships and Fellowships in Agriculture

The Agricultural Research Council has issued a useful booklet giving particulars of the thirty post-graduate studentships offered in 1961, tenable for one to three years, and including a limited number of veterinary training grants, of four years duration, given to enable science graduates to read for a veterinary qualification (Pp. 20. London: Agricultural Research Council, 1961). The studentships, which are open to honours graduates in science or those holding a veterinary qualification, or to graduates in agriculture or horticulture who have shown special interests in one of the basic sciences, and veterinary training grants vary from £340 to £520 per annum tax free, together with educational fees. Particulars are also given of three agricultural research fellowships of £700 to £1,000 per annum, tenable for up to three years, offered to honours graduates of not less than three years postgraduate experience, and two veterinary research fellowships of £900, rising to £1,000 per annum, tenable for up to three years, open to qualified veterinary workers with not less than three years experience in veterinary research. The booklet also describes the scope of agricultural research and outlines the openings available to agricultural research and advisory work.

Biographical Material relating to Richard Owen

Prof. Jacob W. Gruber, associate professor of anthropology, Temple University, Philadelphia, Penn., U.S.A., writes: "During the past few months, I have been preparing a catalogue of the collection of Owen correspondence in the possession of the British Museum (Natural History). It has occurred to me that it would be valuable to bring together as many materials relating to the life of Richard Owen as may still be extant. I would, therefore, appreciate any information relating to the nature and whereabouts of such materials".

The Indian Society of Genetics and Plant Breeding

The following have been elected officers and councillors of the Indian Society of Genetics and Plant Breeding: *President*, Dr. E. K. Janaki Ammal; *Vice-presidents*, Dr. A. R. Gopal-Ayengar, Dr. A. B. Joshi; *Secretary*, Dr. M. S. Swaminathan; *Editor*, Dr. B. P. Pal; *Councillors*, Dr. S. M. Sikka, Dr. S. Govindaswamy, Prof. P. N. Bhaduri, Dr. B. S. Kadam, Shri G. P. Argikar, Dr. K. Ramiah.

Royal Society Visiting Professorship

The Council of the Royal Society has appointed Prof. R. Couteaux, professor of animal biology, University of Paris, to be Royal Society visiting professor for the academic year 1961–62. He is expected to take up the appointment on October 1 and work in the Department of Biophysics at University College, London, on the structure and function of neuro-muscular connexions. Prof. Couteaux is a distinguished histologist who has made outstanding contributions by microscopic and histochemical means to our knowledge of synaptic structures.

University News :

Birmingham

THE title of first assistant to the chair of pathology has been conferred on Dr. D. B. Brewer, reader in pathology. The following appointments have been made : Dr. M. Z. Atassi, to be Research Fellow in the Department of Chemistry ; Dr. D. A. Smith, to be lecturer in the Department of Microbiology ; M. J. Hamlin, to be lecturer in the Department of Civil Engineering ; Dr. B. Cockayne, to be lecturer in the Department of Physical Metallurgy.

The thirty-first annual report of the University of Birmingham Research Committee covers the session 1959–60 (Pp. 137+1 plate. Birmingham : The University, 1961). Besides summarizing research progress in the various departments during the session, it gives, arranged by departments under faculties, particulars of work published during the year and titles of theses approved for higher degrees. There is also a selected list of general works and writings by members of the University staff, not included in the departmental research bibliographies ; this is arranged by faculty.

Cardiff

IT has been announced that Dr. H. K. M. Lloyd, at present senior lecturer in metallurgy at the University of Nottingham, has been appointed to succeed Prof. W. R. D. Jones in the chair of metallurgy at the University College of South Wales and Monmouthshire, Cardiff.

London

DR. R. A. SHOOTER, reader in bacteriology at St. Bartholomew's Hospital Medical College, has been appointed to the chair of bacteriology tenable at that College. Mr. L. H. Hamlyn, lecturer at University College, has been appointed to the University readership in histology tenable at that College. The title of reader in physics in the University of London has been conferred on Dr. R. O. Davies in respect of his post at Queen Mary College.

Manchester

PROF. B. H. FLOWERS, who has held the chair of theoretical physics since 1958, has been granted the title of Langworthy professor of physics, and will continue to be responsible for the teaching and research in theoretical physics. Two other chairs in physics, one vacated by Prof. Samuel Devons and one recently authorized, have been filled by the appointments of Dr. E. B. Paul (from a date to be arranged) and of Dr. H. E. Hall (from March 1). The following appointments have also been announced : Dr. J. Hoenig, to be reader in psychiatry ; Dr. M. F. Lappert, to be senior lecturer in chemistry. Dr. J. F. Adams has been appointed a reader in mathematics from a date to be arranged.

Announcements

PROF. C. H. TOWNES, professor of physics at Columbia University, has been awarded the Rumford Premium of the American Academy of Arts and Sciences for his work on microwave amplification by stimulated emission of radiation (maser). The award consists of two medals, one of gold and the other of silver, and 5,000 dollars.

LORD NELSON OF STAFFORD has been elected an honorary member of the Institution of Electrical Engineers in recognition of his contributions to the development of electrical science and engineering, and for his services to the Institution.

Julius A. Stratton, president of the Massachusetts Institute of Technology, has been awarded the Faraday Medal of the Institution of Electrical Engineers for his contributions in the fields of technological education and research in radio communication.

MR. P. LAMBERT has been appointed head of the Engineering Section of the British Steel Castings Research Association, Sheffield. Mr. Lambert joined the Association's staff in September 1955, as a senior investigator in the Plant Engineering Section, paying special attention to problems arising in fettling shop operations. During the past year he has been engaged on liaison work with member companies relating to the simplification of work.

THE annual conference of the Institute of Metal Finishing (incorporating the Electrodepositors' Technical Society) is to be held at Llandudno during May 2–6. Further information can be obtained from the Conference Secretary, Institute of Metal Finishing, 32 Great Ormond Street, London, W.C.1.

A METEOROLOGICAL field course is being organized jointly by the Royal Meteorological Society and the Field Studies Council, and is to be held at Preston Montford during April 5–12. The course is particularly designed for sixth-form grammar school pupils. Further information can be obtained from the Assistant Secretary, Royal Meteorological Society, 49 Cromwell Road, London, S.W.7.

THE spring conference of the X-ray Analysis Group of the Institute of Physics and the Physical Society, entitled "The Crystal Structures of Organic Compounds", will be held in the Chemistry Department, University of Glasgow, during April 6–7. Further information can be obtained from the Institute of Physics and the Physical Society, 47 Belgrave Square, London, S.W.1.

AN international symposium on "Criticality Control in Chemical and Metallurgical Plant", organized by the Organization for European Economic Co-operation's European Nuclear Energy Agency in collaboration with Kernreaktor Bau- und Betriebsgesellschaft m.b.H., is to be held during May 2–5 at the Karlsruhe Nuclear Research Centre in Germany. Further information can be obtained from O.E.E.C. European Nuclear Energy Agency, 38 Boulevard Suchet, Paris 16e.

THE fifth European Congress on Molecular Spectroscopy is to be held in Amsterdam during May 29–June 3. The Congress is being sponsored by the International Union of Pure and Applied Chemistry, the Koninklijke Nederlandse Chemische Vereniging and the Nederlandse Natuurkundige Vereniging. Further information can be obtained from Dr. D. H. Zijp, Anorganisch Chemisch Laboratorium, Nieuwe Achtergracht 123, Amsterdam-C, Netherlands.

ERRATUM. The recent announcement concerning Dr. D. C. Rose in these pages (*Nature*, **189**, 444; 1961) is incorrect; Dr. Rose has in fact been appointed associate director of the Division of Pure Physics of the National Research Council, Canada.

THE NATURE CONSERVANCY

ANNUAL REPORT

THE eleventh annual report of the Nature Conservancy, covering the year ended September 30, 1960*, records a number of encouraging features to which reference is made on p. 779. Planning and initiating scientific management on the national reserves continued to be a major activity and the six new management plans approved by the Conservancy during the year brought the total of reserves managed under plans to 39, or nearly half the total declared. In Scotland 16 out of 24 declared reserves are now managed under approved plans; in England 19 out of 42; and in Wales 4 out of 17. High priority was given to increasing the cadre of field-staff such as warden naturalists, wardens and estate workers, but outside assistance is still needed. Another major task of the conservation staff is concerned with the sites of special scientific interest, and in England and Wales the revision of county schedules, timed to coincide with quinquennial revisions of county development plans, is now well advanced. Four new national Nature reserves were established during the year: 2 in Scotland, 1 in Wales and 1 in England. With 4 extensions, the 84 reserves at the end of September covered 138,991 acres.

During the year, 10 new grants for research, totalling £7,173, were approved, and 7 existing grants were extended or renewed, bringing the expenditure on grants to some £16,529 compared with £10,217 a year ago. Fourteen studentships were awarded, 20 were continued and 6 applications for third-year extensions were approved. Lists of these research grants and studentships, with lists of reserves, publications and of the Conservancy's committees are appended to the report. With special grants from the University Grants Committee, a one-year postgraduate diploma course in conservancy was set up at University College, London, and 6 additional studentship awards were made to enable the 6 students accepted to attend this course.

Scientific research again covered a wide field. At Merlewood Research Station, the major research continued to be on woodlands and particularly to elucidate as fully as possible the biological and physical processes in which the soils and living organisms of a woodland are involved, more especially the amounts of nutrients for plant-growth available in the soil, the rate at which they are taken up, and the processes by which the supply is maintained. An important part of the work in this field was carried out in three sets of forest plots, at West Tofts in the Breckland, Abbotswood in the Forest of Dean and at Bedgebury in Kent; and from the observations obtained it was possible to draw up a major part of the balance sheet for nutrients in the plots and to assess the productivity of the different tree species. These investigations show that losses of nutrients from the ecosystems of forest plots which are incurred by the felling and extraction of the stems are not so great as for agricultural crops, the most serious potential losses being those of phosphorus and calcium. Some badly needed information on the rate of supply of minerals by soil weathering and the rate of loss by leaching may in the future be acquired from the experimental plots at Gisburn Forest, set up jointly by the Forestry Commission and the Nature Conservancy. The present work of the Plant Soil Section is concentrated on the study of the nutrient cycles in irregular woodlands of semi-natural structure, and along with studies on breakdown of litter an extensive survey has been made of woodland soil animals. To facilitate comparisons of the nutrient cycles and productivities of natural and managed woodlands, an attempt is being made to provide samples of woodland resembling what is believed to be the natural state.

At Moor House, besides continued work on the productivity of grasslands and the growth of tree species in upland areas, a broad survey of the plant ecology of such areas was commenced and a geological survey, including a map of the reserve and an outline investigation of the peat stratigraphy and vegetation history, as shown by pollen analysis, is almost ready for publication. Investigations on the mountain grasslands and soils of Snowdonia also continued, and in the study of soils attention has been given to the distribution of iron within them, while work continued on the trace element content (particularly of cobalt and copper) of soils of direct interest to the research programme as a whole. Differential grazing experiments at Cwm Idwal and on the south-east slopes of Snowdon show that, with complete protection from grazing, *Calluna vulgaris*, *Vaccinium myrtillus* and *Erica tetralix* are increasing on the more acidic soils, and taller-growing grasses, such as *Deschampsia caespitosa* on the more basic sites, though, in such instances, some of the former groups of species are gaining a foothold. A detailed study has commenced of the connexion between the considerable differences in climate and vegetation within Scotland, and the work of re-establishing and encouraging the regeneration of woodlands on nature reserves in Scotland continued to expand. The latest evidence arising out of the work of recording of chalk grassland transects in southern England is that, despite control measures, rabbits have returned in such numbers on a few sites that their grazing is reversing the changes in vegetation.

Work on the ant population of east Dorset heathland at Furzebrook indicates that the effect of fire has been to destroy their population directly and indirectly in various ways, or that they are now spread more thinly over a greater area. Investigation of the food and population cycle of the short-tailed vole (*Microtus agrestis hirtus*) at the Carron Valley will be completed during the present year. A new Unit of Grouse and Moorland Ecology was set up in co-operation with the University of Aberdeen. The pilot red grouse inquiry financed by the Scottish Landowners' Federation indicated that grouse numbers are usually controlled by the birds themselves, and the main problem before the Unit is to discover

* Report of the Nature Conservancy for the year ended 30th September, 1960. Pp. vii+138+14 plates. (London: H.M. Stationery Office, 1960.) 6s. 6d. net.

how the limits to numbers are set. Ecological research on British reptiles continued at the Furzebrook Research Station, and the programmes of marking grey seal (*Halichoerus grypus*) pups on the Farne Islands, the Pembrokeshire coast and in the Hebrides have been more closely co-ordinated. An analysis of all results to date undertaken in consultation with the Zoological Society of London showed that the maximum period between the marking and the recovery of a seal is no more than 61 weeks.

In coastal research, experimental studies at Orfordness demonstrated that the movement of beach material on any coast is not necessarily uni-directoral. The work at Newborough Warren, Anglesey, has now established that the continued mobility of the dunes produces a cyclic interchange between the marram grass community of the dunes and the creeping willow community of the slacks, which could have a period of about 80 years in parts of the dune system at Newborough, although the cycle may be interrupted or extended at any stage by associated changes in the surrounding dunes. The importance of climatological research is also stressed. The Climatological Section at Aviemore provides observations and advice for other research sections and for conservation and regional officers concerned with managing the reserves; and the Moor House Reserve is of exceptional interest as being possibly on the very threshold of climatic conditions suitable for blanket fog development and maintenance, and this and similar thresholds are to form a chief line of research in the Climatological Section.

As usual, the work of the Scientific Advisory Services has considerable scientific interest. In hydrology, the Conservancy has some small-scale experiments in progress which can be expected to contribute useful preliminary information on the effects of land management; but there is real need for field experiments on different catchment areas on a larger scale and by a specialized research unit. Formal representations were made to the Minister for Science regarding the risks to wild-life from toxic chemicals used in agriculture, and a Unit has been established to investigate the subject. The Conservancy also views with great concern the increasing disregard by highway authorities of Circular 718 relating to chemical spraying of roadside verges, and has made representations to the Ministry of Transport. The Conservancy also emphasizes the urgent need for continued forethought and action on the part of the fire service, railways, agriculture, the Nature Conservancy itself and tourism and others to initiate research into the causes of fires in forests, heaths and moors, and into the appliances and techniques for their prevention and control. Investigations into the heavy mortality among foxes suggests that seed dressing with dieldrin and similar chemicals may be a cause. An investigation is planned into the food of red deer, and the Conservancy has also stressed the need for a full scientific appraisal of the status of the coypu (*Myocaster coypus*) in Britain.

SELF-REGULATION IN LIVING SYSTEMS

A SYMPOSIUM on "Self-Regulation in Living Systems", organized by Dr. D. K. C. MacDonald, was held at the National Research Council in Ottawa on January 6. More than thirty people took part, and, as at previous meetings (*Nature*, **184**, 239 (1959); **183**, 370 (1959); **187**, 298 (1960)), these represented many different scientific disciplines, including engineering, neurology, philosophy, physics and physiology. The five papers presented all provoked lively discussion.

In the morning Dr. Bernice Grafstein (McGill University, Montreal) first dealt with the reception of peripheral information, that is, how information is carried from the surface of the body to the central nervous system. By way of introduction, Dr. Grafstein described the structure of a sensory neurone, consisting essentially of a sensory nerve ending which receives the external impulse and a long fibre or 'axon' which transmits the signal to the central nervous system. The transmission takes place with finite velocity by means of progressive displacement of electrical charge through the membrane of the axon. This charge displacement involves essentially a positive feedback mechanism and the resulting 'action potential' is consequently an 'all-or-none' event. A neural message consists of a train of action potential pulses, the coding mechanism being the spacing between the pulses. There are different types of sensory endings sensitive to different stimuli, and there is an orderly spatial arrangement of terminations in the cerebral cortex corresponding to different parts of the body. Thus the central nervous system is informed about the nature and location of the stimulus by which nerves are stimulated. The main part of Dr. Grafstein's talk was concerned with the modulation of the pulse-train in relation to the strength and time-variation of the stimulus. Examples of records of action potentials were shown to illustrate that usually application of an external stimulus gives an initial rapid burst of activity followed by a slower steady activity. For many types of receptor it appears that the initial frequency of action potential activity is dependent on the rate of application of the stimulus, whereas the steady final level depends (often logarithmically) on the magnitude of the stimulus.

Dr. Grafstein considered in greater detail the case of the muscle spindle as a sense receptor. By inserting an electrode very close to the spindle (rather than merely measuring the action potential at a distance down the axon) one can measure a local steady potential at the receptor, the so-called generator potential. On application of the stimulus, this generator potential goes through an initial peak to a final maintained level, the initial peak being related to the rate of stretch of the muscle, and the maintained potential depending on the degree of stretch. There is a fair linear correlation between the final frequency of the action potential pulses and the final generator potential-level. Precisely how the stimulus is converted into a generator potential in the receptor is at present unknown. The generator potential signal is passed down the axon as a digitally coded (or perhaps better pulse-frequency modulated?)

train of action potentials, and it appears that the message is integrated and reconverted into an amplitude-coded form in the central nervous system.

Dr. H. K. Hartline (Rockefeller Institute) then described measurements of the action potential in optical nerve fibres. In this case the receptor in the eye contains a protein substance which undergoes a reversible photochemical reaction on absorption of light. A generator potential is then produced (by an undiscovered mechanism) and the message is transmitted to the brain by action potentials in the optic pathway similar to those described above. In this case, the final rate of activity (after the initial burst) is correlated logarithmically with the brightness of incident light. Dr. Hartline's main thesis was to emphasize that data-processing starts right at the receptor and is not confined to the brain. The receptor passes on to the brain only information 'it considers relevant', and, to quote Dr. Hartline, this often involves a terrible distortion of truth, as it accentuates sudden changes occurring in time and space. Dr. Hartline described experiments on the horseshoe crab, the eye of which is a simple structure made up of a number of separate facets or elements. Electrodes are connected to one particular element of the eye so that the output of a single receptor can be measured. It is found that the output from nearby facets are not independent; for example, the response from a particular element decreases when a nearby element is illuminated. There is a linear relation between the decrease of frequency of one facet and the activity above a certain threshold value of another facet closer than a few millimetres. Dr. Hartline had some lantern demonstrations remarkable in their simplicity to show that this same 'distortion of truth' occurs in the human eye also; for example, a wedge the brightness of which as measured by a densitometer varies uniformly between a light and a dark background appears to have a light band just inside the light background and a dark band within the dark background. This to some extent gives the lie to the old adage that 'seeing is believing'.

In the afternoon Dr. Bradford Dunham (International Business Machines) discussed the computer itself as an object of scientific curiosity. He mentioned three ways of studying computers. The first is by formal studies as initiated by Turing thirty years ago; a Turing machine is a conceptual computer obeying a specific set of simple rules, and the object of the exercise is then to see how much the computer can accomplish. Turing's method appears of limited value; in particular, it is difficult to correlate formal studies with practical conditions. The second method of approach is to construct or simulate a 'baby' machine, a small computer with limited range, and to understand as fully as possible its mode of operation in its own little restricted world. The results are again often doubtful in application, as it is usually by no means certain whether particular conclusions are merely a specific consequence of smallness or whether they are indeed of wider validity. The third way of studying the potentialities of computers is to observe how a computer deals with a particular class of problems. Dr. Dunham described experiments made at International Business Machines to programme a computer to perform automatic design, amplifying what he had said at an earlier symposium (*Nature*, **184**, 239; 1959). He pointed out analogies between the method followed by the machine and the nineteenth-century Darwinian theory of design by natural selection in many generations. Dr. Dunham remarked that the method has been used to design parts for a rocket mechanism, and a long discussion ensued.

The following paper was presented by Dr. Rolf Landauer (International Business Machines) on the necessity for friction in decision-making systems. Thermal agitation in a system has two related effects: friction or dissipation of energy, and random impulses or noise. Noise problems have been widely studied and Dr. Landauer considered an example in information theory. Loss of memory of a 'particle' in an information store takes place when thermal agitation is too large in comparison with the height of the potential barrier separating the two alternative positions for the particle. Dr. Landauer mentioned calculations to indicate what was the optimum size for an element in a memory store of given total mass. Most of Dr. Landauer's talk, however, was concerned with friction *per se*. Whenever we have an indistinguishable merging of two streams of particles there must be friction, for without friction the forces on the particles can be described by a field of force only, and this implies that the particle paths are reversible. However, as we wish to 'kill off' the past memory of the particle trajectories, the paths cannot be reversible and so we must have friction in the system. Dr. Landauer argued that if a machine is to make decisions it cannot be acting merely as a table of 'logarithms' in which every situation is allowed for by the designer, but it must contain some processes involving such an irreversible merging of two streams. The work of Szilard on the measuring process was also mentioned; in general, to make a meaningful measurement we must obtain a result independent of the past history of the measuring apparatus, and this necessitates friction in the system, as, for example, the damping of a galvanometer.

The final talk, by Dr. Arnold Burgen (McGill), described up-to-date knowledge of the problem of cellular storage of information. Information is stored in the nucleus of the cell in the compound deoxyribonucleic acid, a complex chain molecule made up of a large number of units or nucleotides. Dr. Burgen argued from chemical data that a simple molecular organism such as a so-called bacteriophage virus (the nucleus of which would contain only one or two molecules of deoxyribonucleic acid) required about 10^4 nucleotides, a cellular organism containing a single chromosome such as a complex bacterium required about 10^8, while the germ cell of a mammal needed about 10^{10} nucleotides. There are four different types of nucleotide which can be arranged in any order on the deoxyribonucleic acid spiral chain. We never find a single chain, but a chain is always accompanied by its complement. Thus an adenine unit on one chain is always cross-linked (by hydrogen bonding) to a thymine unit on the complementary chain, and a guanine unit to a cytosine. This double chain plays an important part in the replication process of the deoxyribonucleic acid and so of the genetic information when the cell divides. It appears that the double helix starts to split from one end and each parent helix then acts as a 'template' to synthesize two daughter helices complementary to the parents. Two separate double helices identical to the parent eventually emerge. This synthesis has recently been carried out in the test-tube, and the postulated mechanism shown to be essentially correct by labelling with tritium and nitrogen-15. Dr.

Burgen went on to discuss the details of how the genetic information was stored in deoxyribonucleic acid, suggesting that it was likely that four bases were needed to represent one piece of information. He finally considered some of the possible effects of a mistake in the replication process, that is, of a mutation. Dr. Burgen's overall aim was to show that there is no difficulty in principle of storing enough genetical and reproductive information in a mammalian germ cell. A. M. GUÉNAULT

BIOGEOGRAPHY OF SOUTH-EAST AFRICA

A SYMPOSIUM on "The Biogeography of South-east Africa" was held at the University of Natal, Pietermaritzburg, during September 7–8, 1960, under the chairmanship of Prof. S. F. Bush. South-east Africa was taken to include Zululand, Natal and the eastern Cape Province. Particular attention was given to the coastal lowlands, and their affinities with East Africa, but a consideration of the more southern and upland communities made it necessary at times to expand the scope of the symposium to include the south-western Cape.

In south-east Africa the relief, which is in the form of a number of ascending steps, is such that, in general, the inland isotherms tend to run in a north-south direction, parallel to the coast (O. Williams). There is a pronounced difference in temperature between the hot eastern coastlands and the cooler interior highlands, and at the same time temperatures along the coast increase gradually northwards. The coastal plain to the north of Lake St. Lucia (28° S.) experiences a mean July (mid-winter month) temperature of more than 18° C., while areas lying above the 4,000 ft. (1,225 m.) contour experience a mean July temperature of less than 13° C.

Rainfall at the coast ranges from about 30 to 55 in. per annum, and is heaviest at the northern and southern districts of the area considered. Inland, on the seaward-facing escarpments, rainfall is about 70 in. per annum, but on the intervening surfaces it is considerably less. Most of the rainfall is received during summer, but this characteristic is far more pronounced inland than at the coast.

The vegetation of the north-eastern coastal plain is floristically of tropical African affinity (A. W. Bayer and C. J. Ward). Practically every tropical family is represented in northern Zululand, often by the same genera and species as in the tropics. In the case of cosmopolitan families, the Zululand genera are the same as, or closely related to, the tropical African genera. On the other hand, predominantly extra-tropical families are poorly represented in north-eastern Zululand.

The north-eastern vegetation is complex, being made up of a number of different ecological associations, which include mangrove forest, swamp forest, dune forest, coast forest, riverine woodland and savanna. In the region between about 27° 30′ and 29° S., but most noticeably in the Lake St. Lucia area (28° S.), there is a heavy subtraction of tropical species in every type of association. Of a representative 408 species of woody plants occurring in north-east Zululand, approximately 130 do not extend farther south of Lake St. Lucia. To the south of this area of marked thinning out, subtraction is more gradual, the truly tropical element in the flora finally disappearing to the south of East London (33° S.). The number of different plant associations also shows a decline to the south of 28° S.: the swamp forest association does not extend farther south of 30° 45′ S., and the mangrove association terminates at 32° 15′ S.

As the tropical flora becomes impoverished, it becomes admixed with a number of South African species which are not found in north-eastern Zululand.

Regarding sedges, the majority of water-loving species extend from the tropics (where they are distributed across the continent from west to east) through Mozambique and Southern Rhodesia, to the Transvaal, Natal and the Transkei to about 33° 30′ S. (K. D. Gordon-Gray). To the south there is a narrowing of the zone occupied by these plants, so that south of the Natal border only a coastal distribution pertains. In Natal, the majority of the species extend up the river valleys to the foothills of the Drakensberg, but do not appear to cross this mountain barrier into Basutoland and the Orange Free State.

The 'dry-land' sedges follow approximately the same distribution southward, except that they are limited to the drier, and sometimes the higher, land of Southern Rhodesia, and are probably not represented at all on the coastal plain of Mozambique. Annual species, which can more easily overcome the unfavourable season than can perennials, are more widespread from east to west, but they also do not usually extend farther south than 33° 30′ S.

Generally, it may be stated that in this southward 'funnelling' down of the tropical Cyperaceae, there is a marked decrease in the number of species, many tropical species not at present being known from farther south than the St. Lucia area. There is also a marked decrease in the variety of plant forms south of Lake St. Lucia, and a decrease in plant size and inflorescence branching, accompanied by an increase in tufting of the plants and in leaf-blade development.

A temperate sedge flora exists in the south-western area of the sub-continent. This flora extends northwards, particularly along the high ground, and intermingles with the tropical element in Natal. In addition, Natal has its own endemic species.

The freshwater fish fauna of south-east Africa appears to be a very recent fauna, possibly entirely post-Pleistocene, in marked contrast to the temperate fish fauna of the south-western Cape (R. S. Crass). The south-east African fish fauna is clearly tropical in its affinities. Nineteen of the 28 species which occur in the lower Pongolo River (27° S.) extend northwards at least to the Zambesi. Of the remaining 9, 5 are restricted to the eastern Transvaal and the Natal lowlands. These 10 forms may be considered sub-tropical, and are taxonomically closely related to species found farther north.

No strictly freshwater south-east African fish extends south of the Natal border, progressive impoverishment of the fauna occurring southwards. At family-level this trend is illustrated by the fact that out of 14 families found in the Zambesi, only 9 reach the Pongolo (27° S.), 4 the Tugela (29° 15′ S.), and 1 the Umtamvuna (Natal border). This impoverishment does not constitute a true subtraction of the tropical fauna southwards; it is more in the nature of a diffusion gradient which reflects the difficulty experienced by the recent fish fauna in moving southwards across divides between the west-to-east flowing rivers.

Only 13 species occur in the Natal highlands. Of these, 8 are tropical or sub-tropical species, while the remaining 5 may be regarded as temperate, since they are restricted to the cooler highlands. One of these is distributed from the eastern Transvaal to the main Cape watershed, but the others do not extend to the Cape.

The amphibian fauna of north-eastern Zululand is almost identical with that of the lower Zambesi-Beira area, both in its composition and in number of forms (J. C. Poynton). However, in the Lake St. Lucia area, the number of tropical forms drops from 35 to 15. Subtraction farther south is more gradual, but only one form reaches as far as Knysna (34° S.). This subtraction margin is best developed in the coastal lowlands: the tropical fauna becomes markedly thinned out as the land rises from the coast.

South of Lake St. Lucia, the fauna changes from an almost purely tropical to a heterogeneous assemblage, for those tropical forms which pass Lake St. Lucia become joined by a 'South African' fauna, made up partly of sub-tropical Natal-eastern Cape endemics, and partly by members of a temperate fauna[1] centred in the south-western Cape. The subtraction margin of this latter fauna is best developed in the highlands.

The natural distribution patterns of the higher vertebrates have been profoundly upset by human settlement and cultivation, but overall trends are still evident. The tropical element in the avian fauna of north-eastern Zululand is very conspicuous, but there is a marked subtraction of tropical forms in the region of Lake St. Lucia (J. Vincent). Of the 33 species which extend down into Zululand and Natal, but which have no sub-species resident farther south, 17 reach their southern limitation in the St. Lucia region. Elsewhere, subtraction is gradual, but none of these species at present occurs south of Durban.

The majority of tropical mammals occurring in southern Africa show a general distribution pattern which roughly coincides with savanna areas (J. A. Pringle). In the east, this distribution 'funnels down' and extends as a narrow strip along the coast from northern Natal to the south-western Cape. Subtraction of the tropical forms occurs along this 'funnel'. About half the tropical species of Chiroptera and Insectivora do not extend as far south as Natal, the reduction in the number of species apparently beginning in northern Mozambique. On the other hand, most of the Carnivora have a much wider range, and reach Natal. In each of these three groups, the number of tropical species shows a two-thirds reduction between St. Lucia and Port St. Johns (31° 38′ S.), and only a small number in each group extend as far as Cape Town.

The same tendency to 'funnel down' the south-eastern lowlands and extend to the south-western Cape is shown by the tropical rodents (D. H. S. Davis). A southward subtraction is shown in this area. A small 'southern African' element is also represented in this group.

Concerning invertebrates, it appears that the main route of migration from the African tropics is also down the eastern half of southern Africa, but this applies chiefly to groups which have strong and active members which are able to distribute themselves by their own bodily activities, and which are not particularly dependent on the humidity factor (R. F. Lawrence). The position with regard to the humidity-dependent groups is quite different, the tropical and South African faunas having little in common. In the harvest-spiders, for example, the dominant family in tropical Africa is not the dominant family in South Africa, and neither region has a single species of these families in common with the other. The dividing line is the Limpopo region. Again, the South African Onychophora have nothing in common with the tropics, where only one species of a quite different family occurs. In both the harvest-spiders and the Onychophora the relationships of the South African faunas with those of the other continents are greater than with those of the African tropics: their affinities are inter- rather than intra-continental, and latitudinal rather than longitudinal. The cryptic faunas with inter-continental relationships are older, probably very much older, than the groups with intra-continental relationships.

The southern African Diptera also show a marked differentiation into tropical and South African temperate assemblages (H. E. Paterson and B. Stuckenberg). The tropical families tend to funnel down the eastern lowlands, where progressive subtraction occurs. Very few tropical dipterans reach the south-western Cape. The dipteran fauna of the Natal highlands is largely continuous with that of the south-western Cape. This temperate fauna differs strikingly from the dipteran fauna of north-eastern Zululand. The relationships of the temperate fauna are again inter- rather than intra-continental, and latitudinal rather than longitudinal. Some very primitive forms are present in this south-western fauna.

All families of butterflies represented in south-east Africa have a predominance of species in the tropics (K. M. Pennington). Extension of tropical species into South Africa is via the east-coast route, although here the tropical fauna shows a pronounced tapering off. A non-tropical South African fauna is also represented in south-east Africa, particularly in the highlands, where close affinities with the fauna of the south-western Cape are shown.

North-eastern Zululand is very rich in tropical arthropod-borne viruses: in this region 11 viruses have been found to be active (P. Weinbren). From Lake Sibayi (27° 20′ S.) southwards, however, the general virus activity tails off abruptly, and there is evidence of only 3 of the above viruses in Natal. At Knysna, however, 6 of these viruses have been found, producing a pattern which is in contrast to the usual pattern of continued subtraction southwards.

Through the great diversity of groups considered at this symposium, a close conformity of distribution patterns seems unmistakable. The flora and fauna of the northern Zululand plain is truly tropical:

in the north-east, South Africa possesses an almost fully developed tropical East African association. However, in South Africa this association is very definitely restricted to a small area. A well-marked southern 'boundary' is evident in the region of Lake St. Lucia, there being a most pronounced subtraction of tropical species in this region. The factors causing this southward limitation have still to be clarified. The cause of the western limitation of the tropical assemblage inland is explainable in terms of physiography, the ascent to the central plateau causing profound changes in climate; but there are no comparable physiographical changes in the St. Lucia region. There are also no abrupt zonal climatic changes in this region, although it seems significant that the 18° C. mid-winter isotherm crosses the coastal plain in this region, after skirting the western edge of the Mozambique plain. This isotherm is used to divide a tropical from a non-tropical climate in Köppen's classification of climates[2]. Phytogeographical changes in this region are not in themselves sufficient to account for the general changes in the fauna, for although the taxonomic changes in the vegetation are extremely marked, the physiognomic characters of the various plant associations are not conspicuously altered.

Whatever the factors causing the biogeographical changes in Zululand may be, it is evident that the widely held belief that "There is a strong, general reduction of the (tropical) fauna northward into the Sahara and a less strong reduction and some differentiation southward into South Africa[3]" is a serious under-estimation of the extensiveness and importance of these changes. The south-east African plant and animal communities are evidently built up from three quite distinct elements: a tropical complex entering from the north, a warm temperate complex entering from the south-west, and a relatively small complex indigenous to the area. The area clearly shows the characteristics of a transition zone, and this symposium brought into particular prominence the fundamental difference between the flora and fauna of the African tropics and the flora and fauna centred in the south-western Cape. The recognition of the south-western Cape as a biogeographical region distinct from the Ethiopian region is indicated by all the groups which are less recent than the contemporary birds and mammals, the members of which have the added advantage of homoiothermy. Birds and mammals traditionally form the zoogeographer's stock-in-trade; but a proper assessment of the status of the southern temperate region of Africa is only possible if these groups are seen in a balanced perspective.

J. C. POYNTON

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HIGHER EDUCATION IN THE UNITED STATES

DR. J. B. CONANT has recently examined some of the ambiguities between school, college and university in the United States and compared the American approach to the university with that of certain European countries (*Proc. Amer. Phil. Soc.*, **104**, No. 6; December 15, 1960).

Conant believes that the comparison between the large numbers of American youth attending a college or university and the small numbers enrolled in European universities is misleading. A European university is essentially a collection of professional schools. If one compares the percentage of an age-group attending universities in a European nation and those attending American postgraduate institutions, the difference is not very striking.

The road to the university in Europe does not pass through the equivalent of an American college. Instead, there are essentially pre-university schools for those who aim at university education. They offer a stiff academic course of eight or nine years in length centred on either: (*a*) Latin and Greek, or (*b*) Latin and a modern language (or two) and (*c*) modern languages, science and mathematics. In each of the German States, and in each of the Swiss cantons, there are three types of pre-university schools, each preparing students to pass examinations for a State certificate which, in turn, provides admission to a university anywhere in the country.

The American liberal arts college is in the nature of an accident. During the nineteenth century the programmes which were offered for the first degree in arts or science, or in letters, were expanded to include a number of practical subjects. This fact makes it difficult to explain to a European what is meant by an American college. Within a university, too, there is a great variety of four-year programmes of study which may be entered directly by high-school graduates.

An American college is possibly intermediate between a high school and a 'university' in the European sense of the word. For the most part, those who become lawyers now study three or four years in an undergraduate department of a university, or in a four-year liberal arts college before they enrol at a law school; the same is true of medical students. On the other hand, engineering schools never became postgraduate schools. As a consequence, high-school graduates enter directly on their professional training if they want to become engineers. With so many complications in mind, it is hard to define without ambiguity the relation of a college to the education of members of the learned professions.

There is another ambiguity inherent in the American pattern of higher education. The standards of admission to the American colleges and universities are so varied as to make it impossible to describe them accurately.

Standards for the first degree are almost as diverse as the standards of admission; the mere holding of a bachelor's degree has almost no significance. Yet no one would publish a rank list of institutions or even be willing to be quoted publicly to the effect that a straight '*A*' record in one college has about the same meaning as a '*C*' record in another. In the United States, there is a hierarchy of institutions granting the first degree and a complete conspiracy of silence as to the existence of such a hierarchy.

On entrance tests, Conant recommends that leading professional schools of law and medicine and graduate

schools of arts and sciences might require their candidates to pass a set of examinations which would demonstrate a mastery of academic subjects somewhat comparable to that required for entrance into a European university. The requirements might be as follows: a good reading, writing and speaking knowledge of at least one foreign language; a knowledge of mathematics as far as the calculus; a knowledge of physics, chemistry and biology at the freshman college-level; the ability to write a competent essay; a knowledge of American history and political constitutions at a sophisticated level; and a knowledge of English and American literature at a corresponding level.

The variety of colleges prevents any uniform set of standards for admission. Therefore, the colleges could not, even if they desired, greatly influence the high-school curricula. But the relatively homogeneous nature of the graduate and professional schools makes the formulation of standards possible. The effect of this formulation would influence both colleges and high schools.

CIRRHOSIS OF THE LIVER IN FRANCE

An investigation was recently undertaken by the nutrition department of the Institut national d'Hygiene, Paris, into the role of alcohol in the ætiology of cirrhosis of the liver in France (*W.H.O. Chronicle*, **14**, December 1960).

Cirrhosis of the liver is relatively more common in France than in the rest of Europe; the death-rate in 1956 was the highest in Western Europe (32·5 per 100,000 inhabitants, as against 2·6 in England and Wales and 13·6 in the Federal Republic of Germany). For many years the medical profession in France has attributed the high incidence of the disease to the excessive consumption of alcohol, and statistics from hospitals agree that 80–85 per cent of cirrhoses are alcoholic in origin. But the medical profession has been accused of prejudice, and wine merchants have put forward the argument that in a population of whom 80 per cent are drinkers, it could be maintained that practically all illnesses are alcoholic in origin.

The survey was designed to answer five questions: did persons believed to have cirrhosis of alcoholic origin drink more before their illness than random controls of the same age, same sex and same social environment without cirrhosis; were they less well nourished (that is, is cirrhosis due to alcohol or to an associated nutritional deficiency); is the reduced food intake so often seen when cirrhosis becomes decompensated a cause or a consequence of the decompensation; can the amount of alcohol that causes cirrhosis be determined; and what part does wine play in the alcoholism of cirrhotics?

The survey was carried out in hospitals in Paris, Marseilles, and Nantes, all patients with alcoholic cirrhosis being questioned and a non-cirrhotic control being chosen at random in the same department for each patient questioned. The physical activity at work and outside work, the height and the usual weight before cirrhosis began were recorded, and a detailed food questionnaire was devised to establish the daily food intake before and after the onset of the disease, as well as the quantity of alcohol absorbed daily. In addition, questions were asked to reveal the social background about the patients' family and parents, income, living conditions and standard of living.

In all, 116 cirrhotics and 116 controls were compared. They did not differ significantly in age, physical activity, weight, or calorie or protein intake; but the alcohol intake of the cirrhotics was found to be approximately 2·5 times greater than that of the non-cirrhotics. Before they fell ill, the cirrhotics has been just as well nourished as the others; consequently, it was concluded that cirrhosis cannot be attributed to dietary deficiencies.

Only one out of the 116 patients with cirrhosis said that he had consumed less than 80 gm. of alcohol (that is, less than 1 litre of wine at 10°) daily. From this it may be inferred that alcoholic cirrhosis appears only when consumption of alcohol is greater than 1 litre a day. But 50 out of the 116 controls consumed 80–160 gm. of alcohol a day (1–2 litres of wine), and it was only in the category from 160 gm. of alcohol (2 litres of wine) up that controls tended to decrease in number (7 out of 116), while more than half the cirrhotics (64 out of 116) came within this range.

It seems reasonable to infer that cirrhosis is likeliest when the intake is between 2 and 2·5 litres of wine a day (172–212 gm. of alcohol). Cirrhosis can occur when it is 1 litre or more, but when it exceeds 2 litres the probability of its occurrence is much increased.

Is decreased food intake a decompensating factor in cirrhosis? Apparently not to any marked degree: in 88 cases out of the 116 it failed to cause decompensation; thus even at this late state the nutritional deficiency is only associated, not causal.

Finally, the survey established that wine represented 80–90 per cent of the alcohol ingested.

ELECTROLYTIC JUNCTION WITH AMPLIFYING PROPERTIES

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In previous papers[1,2] it has been shown that the rectification of alternating electric current at a junction of two electrolytes is possible. This is analogous to the same effect at a junction of *n*- and *p*-type semiconductors. It is to be expected that other effects in semiconductors, for example, the amplification of electric current, have analogies in electrolytes. The purpose of this article is to report that this has been achieved.

The electric circuit is similar to that used with Ovitron amplifiers[3]. The essential difference between the Ovitron and the device reported in this article is

that the active parts of Ovitron amplifiers are metal-metal oxide electrodes, and here electrolyte-electrolyte junctions.

The device (Fig. 1) consists of two rectifying elements of the type described earlier[1], turned face to face in such a way that, in the ideal case, alternating current in the main circuit could not pass through. Each of the rectifying elements consists of two ion-exchange membranes: cation in H^+ form and anion in OH^- form ('Zerolit permaplex' *C*-20 and *A*-20, respectively, United Water Softeners, Ltd., London). A thin, perforated polyvinylchloride sheet (0·025 mm. thick) is placed between the membranes to reduce the active surface of the rectifier. Ion-exchange membranes are always wet, due to sheets of filter paper soaked in pure water, and attached to the membranes. The whole device is held together with three pieces of graphite, which also serve as electrical connexions.

Electric impulses (direct or half-wave rectified current) in the second, 'impulse' circuit pass through rectifying elements in forward direction. A full-wave rectifying tube, used as double diode, and a high resistance in that circuit prevents the flow of alternating current from the main circuit. The impulses from the impulse circuit cause the rectifying elements to become 'conductive', and the amplification of the current is observed as the result. The current in both circuits is measured on milliammeters (I_1, I_2), and the current in the main circuit is also followed on a cathode ray oscilloscope screen. Alternating current (50 cycles per sec.) is applied in the

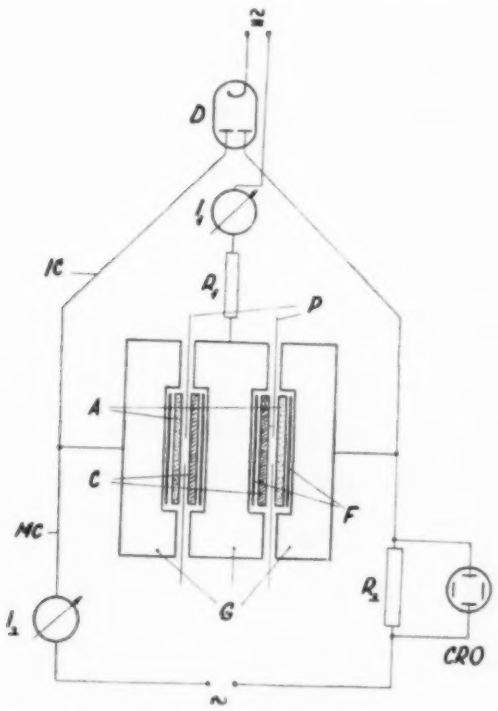

Fig. 1. Schematic presentation of device: *IC*, impulse circuit; *MC*, main circuit; *A*, anion exchange membranes; *C*, cation exchange membranes; *G*, graphite pieces; *P*, polyvinylchloride sheets; *F*, sheets of filter paper; R_1, R_2, resistances; I_1, I_2, milliammeters; *D*, double diode; *CRO*, cathode ray oscilloscope screen

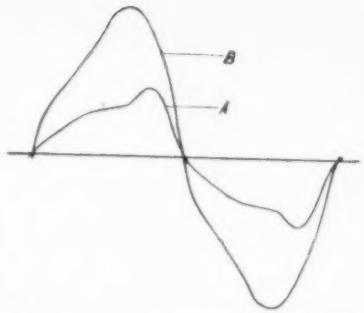

Fig. 2. Typical curve with direct current in impulse circuit: *A*, current in the main circuit before impulse is applied; *B*, current in the main circuit during the impulse

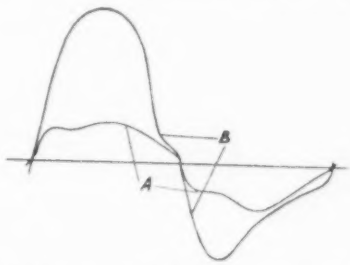

Fig. 3. Typical curve with rectified sinusoidal alternating current in impulse circuit: *A*, current in the main circuit before impulse is applied; *B*, current in the main circuit during the impulse

main circuit. The pulsating voltage in the impulse circuit is obtained from alternating current of the same frequency and phase as that in the main circuit by passing through the diode. If the current passing through the main circuit has not exactly the sine form, the milliammeter does not show the right value. Therefore the curves on the cathode ray oscilloscope screen are photographed and the exact values of the current obtained by integration.

In each experiment, first the current in the main circuit is determined (it is different from zero, because of non-ideal rectification). Then, the impulse circuit is switched on, and immediately the current in the main circuit is determined again. The impulse circuit remains closed until the current in the main circuit stabilizes (1 min.). The stabilized current is determined, the impulse circuit cut off, and the current in the main circuit, in 'unconductive' state, is determined again.

The amplification is obtained by means of the equation:

$$\text{per cent amplification} = \frac{i_m - i_g}{i_g} \times 100$$

where i_m = the increase of current in the main circuit, and i_g = the current in the impulse circuit.

When the direct voltage in the impulse circuit is applied, the amplification, immediately after closing this circuit, is about 60 per cent and, after stabilization, about 100 per cent. In the case when pulsating voltage is applied, amplifications of 45 per cent and 80 per cent are obtained. Typical curves with direct and pulsating current are shown in Figs. 2 and 3.

Curves *A* in Figs. 2 and 3 represent non-ideally rectified alternating current. Both halves of the cycle are equally distorted, because the current passes

through two rectifying elements, turned face to face (Fig. 1). The current increases symmetrically in both halves of the alternating-current cycle if direct current is applied in the impulse circuit over the full alternating current cycle (curve *B*, Fig. 2). If the impulse is a half-wave rectified sinusoidal alternating current of the same frequency and phase as that in the main circuit the situation is different (Fig. 3). The first half of the main circuit alternating-current cycle is that in which the impulse is applied, and an increase of the current is observed. But an increase is also observed in the second half of the cycle, where no impulse is given (curve *B*, Fig. 3). In such cases evidently the amplification has a certain time-lag. This 'frequency-response' of such systems is very interesting, and it is the object of further investigations.

In both cases (direct or alternating current impulse), the current in the main circuit not only increases but also the shape of the curve approaches the sinusoidal form. This is strong evidence that the amplification is a consequence of a diminished rectifying action, caused by an electrical impulse, which impels the ions toward the rectifying interfaces.

We wish to thank Dr. I. Hruska for helpful discussions of this work.

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SOME FACTORS INFLUENCING THE FOOD-CHAIN TRANSPORT OF RADIOACTIVE MATERIALS INTO COW'S MILK

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VARIATIONS in the radioactive contents of milk have been observed and have been variously attributed to seasonal influences, changes in feeding practices, varying contamination-rates, etc.[1-4]. No detailed explanation of the fundamental principles underlying these variations has yet been presented. The following approach provides a method by which such variations can be explained.

The discussion is based on the fact that cows are fed on grass, hay, etc., which, prior to its consumption by the animal, has been exposed to radioactive contamination over a period of time. The general applicability of the proposed method will be shown in three model cases which illustrate three combinations of basic conditions:

I. (*a*) Constant feeding conditions throughout the year; (*b*) contamination of the fodder with radioactive material at a constant rate. II. (*a*) Constant feeding conditions throughout the year; (*b*) contamination with radioactive material at a varying rate. III. (*a*) Seasonal variations of feeding conditions; (*b*) contamination with radioactive material at a constant rate.

Two assumptions are made in order to simplify the presentation: (*A*) Contamination of milk is assumed to be essentially proportional to the contamination of the diet of the cattle. (*B*) Contamination of the diet is assumed to be essentially proportional to the product of the rate of contamination by the time of exposure.

Other factors which influence to some degree the contamination of fodder and milk are not introduced in the discussion of the three model cases because they do not affect the basic considerations.

In the graphic presentation of the three model cases I, II and III (Figs. 1 and 2) twelve successive conditions *A*–*L* are shown for each of these model cases. In each sub-graph of this presentation the abscissa gives the time-scale while the ordinate

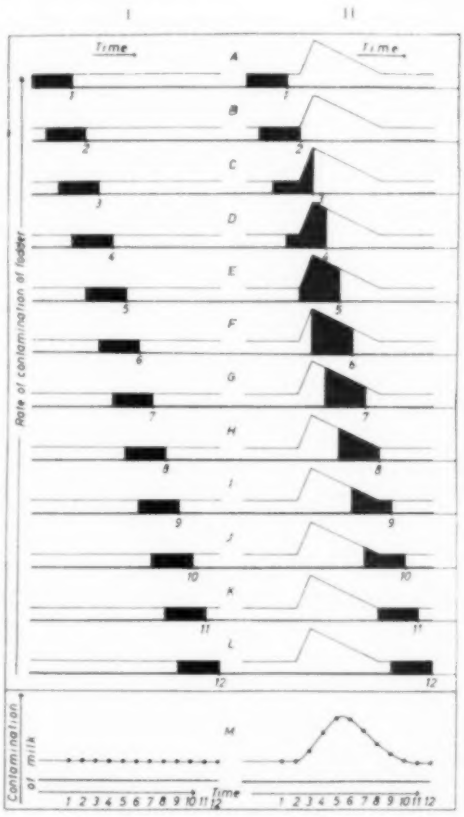

Fig. 1

III

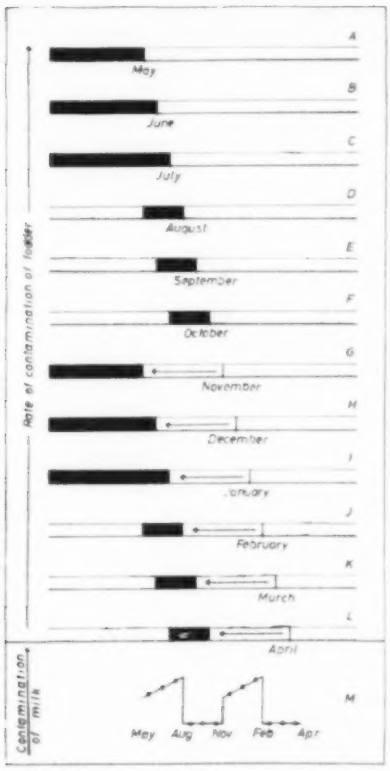

Fig. 2

indicates the rate of contamination. The total amount of radioactivity supplied with the grass to the cattle at times 1–12 is shown by the shaded areas in sub-graphs *A*–*L*. Sub-graphs *M* show the resulting contamination of the milk as a function of time.

The graphic presentation in model case I (constant feeding conditions, constant rate of contamination) shows clearly that the contamination of the milk remains constant, as shown in sub-graph (I) *M* of Fig. 1.

In model case II (constant feeding conditions, variable rate of contamination) the rate of contamination is assumed to rise gradually to a maximum at time 3, slowly returning to 'normal' at time 8. The cows feed on grass contaminated by amounts of radioactivity equal to the shaded areas of sub-graphs (II) *A*–*L*, respectively. At time 3 they consume grass which has for a considerable time been exposed to contamination at a low rate and for some time to contamination at a high rate. The total accumulated contamination of the grass ingested by the cattle at time 3 for that reason is somewhat higher than at times 1 or 2. Thus contamination of milk will increase until a maximum is reached between times 5 and 6. Later, milk contamination decreases again, and at time 11 it reaches its original value.

The result is demonstrated in sub-graph (II) *M*: the maximum rate of contamination at time 3 causes a maximum of milk contamination at times 5–6.

Model case III, shown in Fig. 2, illustrates a typical case approximating conditions in a country where the feeding conditions change with the seasons. The rate of contamination of the fodder is assumed to be constant.

Sub-graphs *A*–*L* illustrate the following pattern of feeding conditions: cows are kept in a barn until May. During this time they are fed on hay harvested during the previous year. In May they are led to the pasture (sub-graph *A*). The grass they feed on from May until July has not been cut since November of the previous year and has been contaminated at a constant rate (sub-graphs *A*–*C*). By August the cattle return to pastures which have already once been grazed in spring. They start eating grass grown since May and thus exposed to the constant rate of contamination for three months only. They feed on this pasture from August until October (sub-graphs *D*–*F*). After this time, they return to the barn and are again fed on hay harvested between May and July, as indicated by the arrows (sub-graphs *G*–*I*), and between August and October (sub-graphs *J*–*L*), respectively.

Sub-graph *M* of Fig. 2 shows the resulting contamination of the milk from cattle fed under these conditions. It shows that two distinct peak periods of radioactive contamination must exist during the year, even though the rate of contamination remains constant.

The above analysis has not taken into account the influence of variations in food composition. In practice, in many countries of the northern hemisphere, cows are fed on mixtures of hay and concentrates from November to April. These concentrates, consisting of oil cake, etc., contain as a rule very little contamination. For this reason the November–January peak-level should be lower than the May–July peak-level, and the February–April values should be lower than the August–October values. Hay, on the other hand, is not always fed in the sequence in

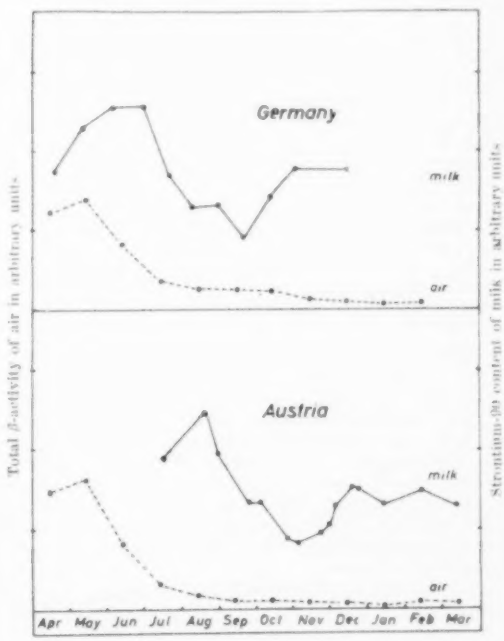

Fig. 3. Radioactivity of milk and air 1959/60

which it was harvested, and this will tend to level off differences between the values for the periods November–January and February–April. In addition, we have to consider the influence of varying deposition-rates superimposed on the seasonal variations of feeding conditions.

In order to demonstrate the applicability to actual conditions of the theoretical considerations discussed in the three model cases, Fig. 3 is presented. It shows the results of measurements of strontium-90 in milk from German and Austrian sources carried out in 1959 and 1960 at the Bundesforschungsanstalt für Milchwirtschaft, Kiel, and at the provisional laboratory of the International Atomic Energy Agency, respectively. These values are shown in relation to results of measurements of radioactivity in air[5,6].

In Germany and Austria conditions are comparable to those considered in model case III. The reasons for the delay between the appearance of a maximum of radioactivity in air and a corresponding maximum of contamination in milk have been discussed in model case II.

Similar results have been reported from sources in the United Kingdom, Canada and the United States[7–10].

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DIQUAT AS AN ARBORICIDE

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SODIUM arsenite has been widely employed as an arboricide and herbicide, but in various countries its use is being progressively restricted or prohibited. Investigations are being carried out at the West African Institute for Oil Palm Research with a variety of herbicides and other chemicals to find an alternative to sodium arsenite for poisoning old oil palms prior to, or concurrently with, replanting. So far diquat, a new desiccant and herbicide first described by Brian *et al.*[1], is the only one that has been found to be consistently effective and it is believed that this is the first record of its use as an aboricide.

The palms used in the trials were planted in 1939 and had attained a height of 25–30 ft. During the rainy season diquat was poured into a small, slightly downward sloping hole about 8 in. deep, punched 2–3 ft. from the ground in the trunk of the palm with a crowbar. The hole was then almost filled with water. Two separate trials were carried out, four palms being treated at each dosage-rate. Diquat was introduced at the following rates of active ingredient per palm :

First trial : 20 gm., : 50 gm.
Second trial : 10 gm. ; 20 gm. ; 40 gm. ; 60 gm. ; 10 gm., followed by a further 10 gm. after three weeks.

The effect at rates of 40 gm. and more was very rapid. Within two weeks of poisoning, all palms which had received these high rates had suffered almost complete desiccation of the older fronds and in some cases desiccation had proceeded as far as the central spear. At the 20-gm. rate the symptoms appeared more slowly, but followed the same course. It was evident that 10 gm. is too little to kill an adult palm and two applications of 10 gm. at three-week intervals were less effective than the single application of 20 gm.

After six weeks the fronds in most of the affected palms had collapsed basally and remained cloaking the stem ; in other palms the fronds dried out in their normal position with some fracturing along their length. In all but one palm the spear remained erect but dried out. This is in contrast to the appearance of palms poisoned by sodium arsenite, where the spear usually falls out and the trunk collapses at any point along its length within two months of poisoning[2]. The collapse of the trunks of palms poisoned by diquat is, however, only a matter of time.

One palm receiving 50 gm. diquat was felled three weeks after poisoning. The expanded fronds were all dead ; but the spear and one immature frond were still green. Internally the trunk appeared drier than normal with some pink discoloration of tissues around and below (but not above) the point of injection. A longitudinal section through the growing point showed no abnormal symptoms at that time. At the centre of the rachis of each dead frond, a pinkish brown discoloration was evident which was more advanced distally ; it appeared to have started in the pinnæ and spread backwards. Transverse sections of some leaf bases showed slightly discoloured, water-soaked areas.

Another palm which had received 50 gm. diquat, was felled and examined after five and a half weeks ; all the pinnæ were desiccated, but there were green areas in the spear and in an immature frond. A longitudinal section through the crown showed that the pinkish brown discoloration had spread to the leaf bases. The entire central portion of the rachis was coloured brown and there were roughly circular areas infected by a black rot. The rot appeared to be invading the spear in an irregular manner, some portions remaining green, others becoming desiccated and brown. The rot had penetrated to within a foot above the growing point, and the whole crown emitted a slightly putrid odour.

Three palms in the second trial were felled two months after poisoning. Symptoms in those which had received rates of 20 gm. diquat and more were similar, but the development of symptoms was more advanced at the higher rates. A soft, wet rot was

observed in the trunk, affecting half the area near the point of injection. The tissues between the vascular bundles had completely broken down and this area was demarcated by a dark brown line. The tissue outside this area was obviously not normal, some tissue breakdown having occurred and the colour being a more yellowish pink than in a normal palm. The growing point was found to be completely destroyed by a wet, putrid rot. There was evidence of wide translocation of the poison; sectioning of the roots revealed brown to black discoloration of the vascular strands and a breakdown of cortical tissue.

At present this method of poisoning is expensive, but diquat has proved more effective than sodium arsenite, which, in West Africa, has given erratic results, except at much higher rates than those found necessary in Malaya[2]. The comparative safety with which diquat may be handled and used is an important point in its favour.

The purpose of this article is to direct attention to the arboricidal properties of diquat; the satisfactory results obtained with it for poisoning oil palms suggest that its use in this way may be of wider application. The samples used were kindly made available, as 'Reglone', by the manufacturers, Imperial Chemical Industries, Ltd.

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'ACTIVE CENTRE' STUDIES IN TRYPSIN

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THE understanding of the mechanism of enzyme action presupposes a knowledge of structural elements of both substrate and the enzyme. This is relatively easy for substrates, which are usually of low molecular weight, but has not yet been achieved for any enzyme because of the complexity of the protein molecule. The essential structural requirements of the enzyme are referred to as its 'active centre'. They should be distinguished from those structural elements of the enzyme necessary for the preservation of its native configuration and not participating directly in the binding or activation of the substrate.

In the particular case of trypsin, its substrate requirements were believed to have been solved earlier[1]. Employing synthetic polypeptides, it was reported that trypsin will only catalyse the hydrolysis of bonds involving the carbonyl groups of the basic amino-acids arginine and lysine. This observation, though essential, did not contribute to the knowledge of the active centre of trypsin. Paradoxically, most of our information about the active site came from the discovery that trypsin and its close analogue chymotrypsin act on substrates bearing no apparent similarity with the above-mentioned ones. These are nitrophenyl acetate (NPA)[2] and di*iso*propylfluorophosphate (DFP)[3]. The latter reacts with trypsin and chymotrypsin in a mole-for-mole ratio to give stable inactive products, the *p*H curve of inactivation being similar to that of the enzymic activity. With NPA, chymotrypsin is inactivated, yielding a monoacetyl derivative. At lower *p*H values, for example, *p*H 5–6, the acetyl group is stable in aqueous solution and reactive towards hydroxylamine[4,5], while at *p*H 7–8 hydrolysis occurs, yielding acetate ions and reactivated enzyme. The group reactive towards NPA could also be readily acylated by various acid anhydrides and acid chlorides employed in an equimolar ratio. With trypsin, hydrolysis of NPA is observed, but no inactivation of the enzyme takes place.

The foregoing observations have implicated the seryl and the imidazolyl residues of trypsin as possible functional groups involved in enzymic action. Another approach to the problem of the active centre has been carried out with the aid of reagents specific for various functional groups in proteins. Acylation of amino-groups left the enzyme still active, while esterification of the carboxyl group gave only partially active protein. However, iodination of the phenolic groups and sulphation of the hydroxyl groups rendered the enzyme completely inactive.

This approach lacks the desired specificity, as all proteins possess essentially the same limited number of reactive groups as part of their structure. Accordingly, the key to their specificity is to be sought in the spatial distribution of these groups as conditioned by the general geometry of their molecule, the charge distribution and its fluctuation, and the possibility of resonance and chelation with the substrate. Hence, it is possible to influence the properties of an enzyme through modification of these factors by either blocking accessible reactive groups or introducing new groups into its molecular structure. In this Laboratory such a broader view of chemical modification was taken, since each derivative formed, even though it may still retain enzymic activity, has acquired a new set of properties which differentiate it from the parent enzyme, or any other of its derivatives. For example, the series of acyltrypsins, obtained through reaction of the native trypsin with seven anhydrides of mono- and di-carboxylic acids, differed in their proteolytic and esterolytic activities[6]. Michaelis–Menten constants, *p*H optima and dissociation constants with their inhibitors, ovomucoid[7] and serum inhibitor[8]. All these parameters of enzyme action depend directly, one presumes, on the interaction between substrate and enzyme on the level of its active site. Strikingly enough, in some instances, far greater differences were observed in trypsin properties not related to the active site but to its general molecular dynamics. These are: stability towards acid, alkali and urea denaturation and self-digestion[9], ease of reversibility of heat denaturation[10], electrophoretic and ultracentrifugal properties and isoelectric points[7]. As the reaction under the conditions employed causes mainly acylation of the amino-groups, it is obvious that the reacted amino-

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groups are not indispensable for enzyme action. As they modify it, however, they could be located peripherically to the active centre. A varying area of tryptic active site would also account for the repeatedly observed different effects of chemical modification, when several substrates are used. Most striking is the insensitivity of the active site of trypsin to overall charge distribution on the protein, as the isoelectric point can be changed from 10·8 of the native enzyme to about *p*H 4 of succinyltrypsin, without greatly affecting its parameters of enzyme action.

Earlier work in this Laboratory with citraconyl and itaconyl trypsin has shown that their proteolytic, but not esterolytic, activity increased on incubation at various *p*H values. Obviously, a direct modification of the active site was involved. This prompted us to investigate the early phases of acylation and its effects on proteolytic activity, which were neglected in most previous work. It was observed that the proteolytic activity of trypsin decreases radically, sometimes even completely, within 3–8 min. on addition of various anhydrides, a slow reactivation taking place on further incubation of the acetylating mixture[11]. Both, inactivation and reactivation, are strongly *p*H dependent. Immediate reactivation can be obtained with hydroxylamine.

Acetylation of Trypsin with Acetic Anhydride

Acetylation in sodium acetate. In the first series of experiments the acetylation was carried out by a slight modification of the customary method[12], employing 0·5 *M* sodium acetate buffer rather than a half-saturated solution. The acetylation mixture was maintained at 0° C. and kept uniformly stirred by means of a magnetic stirrer. The proteolytic activity was determined on urea-denatured haemoglobin at various times after the addition of anhydride. The *p*H of the haemoglobin substrate was adjusted to give a final *p*H of 7·8–8·1 on the addition of the acetylating mixture. The concentration of the split products was determined from the absorption at 280 mμ using a Zeiss *PMQ*II spectrophotometer for the activity measurements.

Results presented in Fig. 1 show that there is a slight loss of activity even on addition of one equivalent of acetic anhydride per mole of trypsin.

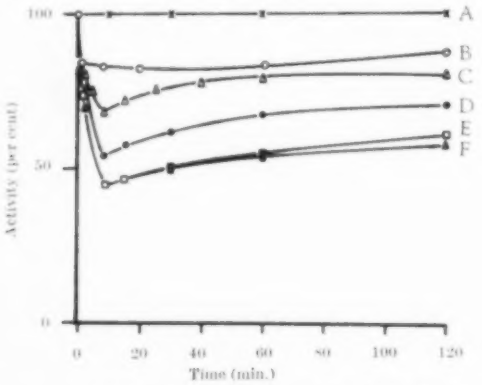

Fig. 1. Acetylation of trypsin with various amounts of acetic anhydride. 5 mgm. of trypsin in 10 ml. of 0·5 *M* sodium acetate was acetylated at 0° C. with: *A*, 80 equivalents acetic acid; *B*, 1 equivalent acetic anhydride; *C*, 4 equivalents; *D*, 20 equivalents; *E*, 40 equivalents; and *F*, 60 equivalents

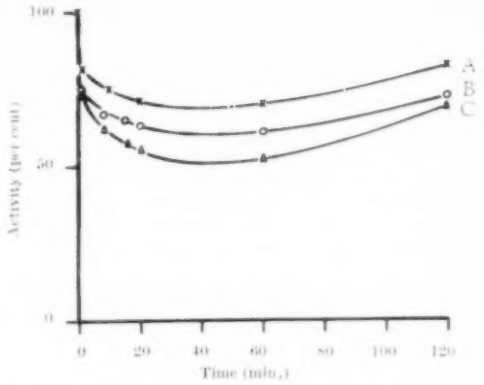

Fig. 2. Effect of buffer concentration. 5 mgm. of trypsin in 10 ml. of solution was acetylated with 40 equivalents of acetic anhydride containing: *A*, 20 mgm.; *B*, 100 mgm.; *C*, 200 mgm. sodium acetate

Maximum loss of activity occurs when 40 equivalents or more of anhydride are employed. There is a serious loss of activity within 1 min. of acetylation. At about 8–10 min. of acetylation, the activity reaches a minimum and begins thereafter to increase. Control experiments show that there is no change in activity on addition of 80 equivalents of glacial acetic acid to the enzyme solution, nor is there a change in activity if acetic anhydride is added to the substrate prior to the addition of the enzyme in amounts corresponding to that present in the enzyme sample used. Customarily, acetylation is performed in half-saturated sodium acetate at 0° C. employing 1·2 ml. of acetic anhydride per gram of trypsin. In Fig. 2 is shown the decrease in activity as the buffer concentration is increased during acetylation. The observed effect is probably due to the increasing alkalinity of more concentrated solutions.

The results of repeated additions of small amounts of anhydride are listed in Table 1. At the first few additions there is a decrease in activity followed by a slow increase. The effect is smaller, however, on second addition, and practically disappears on the third and the fourth. The acetylation of the enzyme during the first addition has an obvious protective effect. The substitution of calcium acetate for sodium acetate did not, however, change the general pattern of the reaction. Similarly, neither did the acetate salts of potassium, magnesium, manganese, barium, aluminium and lead, provided that the *p*H of the acetylating mixture was in the range of 5·5–6·0.

Acetylation at constant p*H values.* The change of the *p*H of the buffer had, however, far greater effects, if, for example, 0·5 *M* buffers of sodium and potassium carbonate, bicarbonate and borate were used. Under these conditions the proteolytic activity approached zero within 1–3 min. on addition of

Table 1. Repeated Acetylation of Trypsin with Four Equivalents of Acetic Anhydride

Time (min.)	Per cent activity			
	First addition	Second	Third	Fourth
0	100	74	76	77
8	77	71	71	76
20	74	73·5	72·5	76·5
30	76·5	76	76	77

anhydride, and, as before, a reactivation took place on incubation of the acetylating mixture[11]. To be able better to explore the dependence on *p*H of both inactivation and reactivation, an automatic titrator was employed in subsequent experiments. The enzyme was dissolved in distilled water and the titrator started at the same time that 65 equivalents of anhydride were added. The *p*H was maintained at the preset value throughout the experiment. The lack of excess buffers permits easier readjustment of *p*H during reactivation studies. In Table 2 is shown the extent of the maximum loss of activity at various preset *p*H values. It is evident that as the *p*H is lowered from 9 to 5 the extent of inactivation decreased from 100 per cent to about 40 per cent. Calcium ions do not have any protective action when acetylation is carried on under the above conditions. The maximum reactivation observed so far amounts to about 50–60 per cent of the native trypsin and to about 80–90 per cent of control samples of acetyltrypsin obtained after exhaustive dialysis and lyophilization. The discrepancy may be due to the fact that trypsin is in equilibrium between a denatured and native form, the latter yielding a fully active acyl derivative while the reversible denatured form becomes irreversibly denatured on acetylation[12].

Table 2. ACETYLATION AT DIFFERENT *p*H VALUES

*p*H	Activity (per cent)			
	0 hr.	8 min.	4 hr.	24 hr.
5	100	62·9	72·5	72·5
6	100	35·1	42·3	42·8
7	100	25·2	44·3	44·1
8	100	0	44·8	44·1
9	100	0	42·7	40·8

The spontaneous reactivation progresses slowly on incubation, but an almost instantaneous reactivation takes place on treatment with hydroxylamine. After 8 min. of acetylation 4 equivalents of hydroxylamine hyrochloride per equivalent of anhydride were added to the acetylating mixture. The hydroxylamine solution was first brought to the *p*H at which the activation was to be carried out and the *p*H of the cnetylating mixture controlled by the automatic titrator. Reactivation was measured after further incubation of 8–10 min. at 0° C. The percentage of reactivation with hydroxylamine as a function of *p*H is illustrated in Fig. 3. Curve *A* shows the extent of activation obtained by spontaneous reactivation without hydroxylamine on incubation of the acetylating mixture at the indicated *p*H values for the same length of time. It can be seen that above *p*H 7 the spontaneous reactivation is not measurable within the incubation period of 8 min. On the contrary, with hydroxylamine (curve *B*) maximum reactivation occurs in the *p*H region of 8–9·5. (Chymotrypsin behaves similarly to trypsin, and its acetylation at *p*H 8 or above results in a reversible inactivation. Maximum reactivation with hydroxylamine takes place in the region of *p*H 7·5–8·0.) This dependence on *p*H of the reactivation is indicative of the presence of O-acetyl groups which react with hydroxylamine in this *p*H region[14]. The spontaneous acid hydrolysis confirms this suspicion. Under the same conditions aliphatic ester, such as ethyl acetate, did not react with hydroxylamine until above *p*H 11, while NPA reacts already at *p*H 6·5 and above. The group present in the enzyme has to have a reactivity intermediate to those of the above two compounds. The spontaneous hydrolysis is far more sensitive to acid than to alkali catalysis.

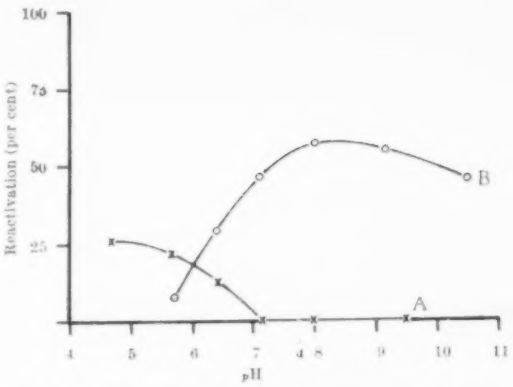

Fig. 3. Reactivation of acetyltrypsin at different *p*H values for an incubation period of 8 min. *A*, spontaneous; *B*, with hydroxylamine

It appeared possible that the imidazole moiety of histidine residues of trypsin can undergo acetylation and spontaneous deacetylation. It is known that acetyl imidazole has a high absorption in the ultraviolet region of 245–260 mμ[15]. Trypsin has 3 moles of histidine per mole of enzyme, and if these groups are undergoing acetylation and hydrolysis, then there should have been a marked increase and a slow decrease in the absorption spectrum at 245 mμ. In Fig. 4 it can be seen that the effect of addition of acetic anhydride to a sample of trypsin (curve *B*) resembles the course of hydrolysis of the acetic anhydride in the same buffer 0·4 *M* borate (curve *A*). The curves were corrected for the absorption of the protein itself. At the same time curve *D* shows an

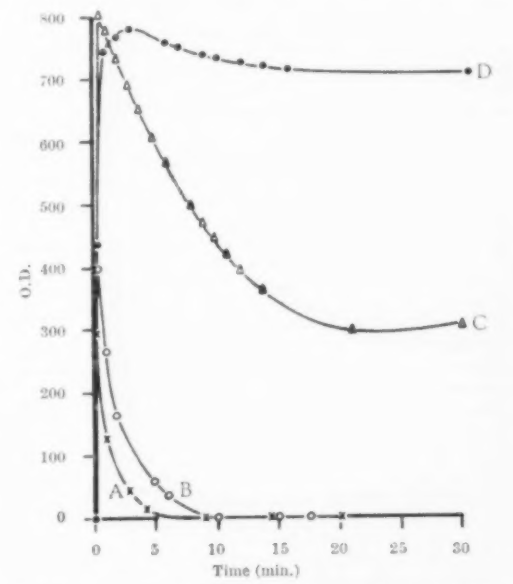

Fig. 4. Change of absorption at 245 mμ during acetylation. *A*, 0·4 *M* borate + 5 mgm. acetic anhydride; *B*, trypsin in 0·4 *M* borate + 5 mgm. acetic anhydride; *C*, histidine in 0·4 *M* borate + 5 mgm. acetic anhydride; *D*, imidazole in 0·4 *M* borate + 5 mgm. acetic anhydride

increase in absorbance from zero to 0·795 on the addition of the same amount of acetic anhydride to a sample of imidazole in a concentration corresponding to that of histidine in the trypsin sample. Curve C indicates the change in absorption of histidine under the same conditions; both these curves are quite different from those obtained with trypsin. It appears, therefore, very unlikely that an imidazole group is involved in the acetylation causing the inactivation of the enzyme, though a role of the group in deacetylation[16] cannot be excluded.

Discussion

Tracer experiments show that DI^{32}P is attached to the hydroxyl group of a serine residue in the reaction causing inactivation of either trypsin or chymotrypsin[17,18]. Kinetic considerations led[19] to the postulation that the same group is acetylated also in the reaction of chymotrypsin and NPA. The resulting monoacetyl chymotrypsin can be isolated[20] and is remarkably stable in acid media, while rapidly hydrolysing between *p*H 7 and 8 (refs. 4 and 5). A variety of acylchymotrypsins was reported to be obtainable by reaction of the enzyme with stoichiometric amounts of acid anhydrides or acid chlorides[4]. All these derivatives are also stable in acid media and hydrolyse in neutral to slightly alkaline media. The dependence of hydrolysis on *p*H (as well as of acetylation of NPA) seems to involve catalysis by a neighbouring imidazole group. Direct spectrophotometric evidence for the intermediary formation of an N-acetyl imidazolyl derivative during the process of deacetylation was presented[16]. Detailed mechanisms for the reaction between the enzyme and NPA were postulated by several authors[19,21,22]. The same mechanism was extended also to the action of chymotrypsin on its normal peptidic substrates, though the evidence for it is largely indirect. For example, the *p*H dependence of hydrolysis of acetyl L-phenylalanine ethyl ester also implicates catalysis by an imidazole group[23]. This mechanism considers proteolytic enzymes as having a transacylating function, with water as the ultimate acyl group acceptor. It is most unfortunate that there is as yet no direct evidence for the actual formation of the acylated intermediates during peptidic hydrolysis.

In its reaction with NPA, trypsin behaves essentially similarly to chymotrypsin[4]. Exact comparison of the kinetic parameters and the *pK* values of the catalytic groups were first presented by Stewart and Ouellet[24]. A stable, inactive monoacetyl trypsin could, however, not be obtained by the authors following the technique used for chymotrypsin. Nevertheless, the rate of hydrolysis of the acetyltrypsin formed increases with *p*H at around neutrality, as shown by stopped-flow technique[24], and was easily confirmed by us.

In striking contrast with the foregoing results are the present results with acetic anhydride. The inactive acetyltrypsin obtained is unstable in acid media, but quite stable in neutral to slightly basic buffers. Similar data were obtained for a variety of other anhydrides[11]. The instability in acid media explains why no inactivation of trypsin could be observed, following the procedure[4] for the reaction of chymotrypsin with acetic anhydride (*p*H 5).

The acetylated group is presumably part of the active centre and is either an aliphatic or an aromatic hydroxyl group. The latter assumption is supported by its reactivity with hydroxylamine, which is intermediate to that of ethyl acetate and those of NPA or phenylacetate. Other groups seem excluded, as Uraki *et al.*[25] have shown that N-acetyl groups are resistant to hydrolysis even under stringent conditions, while the spectrophotometric data presented here preclude the acetylation of imidazole. The difference in *p*H dependence of spontaneous hydrolysis of the acetyltrypsin formed with NPA or with acetic anhydride would imply that two different hydroxyl groups are acetylated and are present in the active site of trypsin. The stability in alkaline media would apparently preclude the possibility that this latter acetyltrypsin is an intermediary in the course of normal enzyme action. An alternative possibility is that the difference in behaviour is due to the simultaneous acetylation of other groups as well, aside from the critical hydroxyl group, by the action of acetic anhydride, but not by the action of NPA. The group acetylated could be a primary amino-group, catalytically active in the deacetylation (and presumably also acetylation) of acetyltrypsin formed by the reaction of trypsin with NPA. This would be in agreement with the results of Stewart and Ouellet[24], who have shown that the hydrolysis of NPA can be catalysed by a combination of a free amino-group and an aliphatic hydroxyl group, namely, lysine methyl ester and *iso*propyl alcohol. The acetylation of the amino-group by the acetic anhydride would eliminate its catalytic role, accounting for the comparative stability of the inactive acetyltrypsin in neutral to alkaline media, while the hydrolysis in acid media may be due to simple acid catalysis. This would explain the difference in the behaviour from chymotrypsin, where an imidazole group has the same catalytic function.

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MECHANISM OF COLLAGEN SYNTHESIS

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EXPERIMENTAL evidence[1-3] indicates that the mechanism underlying the biosynthesis of fibrous proteins, such as collagen or silk fibroin, differs from that operating in the case of globular proteins[4-7]. In this article a mechanism is proposed for the biosynthesis of collagen which could account for the experimental data available at present. This mechanism is based on the notion that collagen is synthesized by an enlargement of the pre-existing collagen fibre by means of the addition of amino-acids or peptide residues and would be analogous to that proposed for hepatic glycogen[8]. The proposed synthetic process is unlike that visualized for globular proteins, which are thought to be synthesized by one continuous process[4-7]. The *a priori* assumption seems reasonable that a long fibrous molecule which is considerably longer than the ribonucleic acid templates[9-11] is probably not synthesized in a single operation but rather by a step-wise addition of simple building blocks. The latter view is supported by direct evidence since it has been observed in this laboratory that the distribution of an isotope among identical amino-acid residues is non-uniform[1,2] after the injection of amino-acids labelled with carbon-14. A similar non-uniform labelling pattern has been found in the case of silk fibroin[12]. It is therefore postulated that discrete regions near the termini of the collagen molecule participate actively in the metabolism of this protein whereas regions distant from these termini are metabolically inert.

By varying the ionic strength or *p*H of the medium, fractions of collagen can be prepared differing from native collagen with respect to their isotope concentration and rate of metabolic replacement[13-18]. Although these fractions have generally been assumed to represent distinct molecular entities within the collagen group, a more plausible, alternative view would be that these fractions originate from the same molecular species of native collagen by a process of intramolecular cleavage. The following evidence may be adduced for the common origin of these fractions: (*a*) all collagen fractions derived from the same organs have almost identical amino-acid composition[19]; (*b*) when collagen is solubilized, the resulting fractions have similar molecular weights[2]; and (*c*) on sub-fractionation of native collagen, C- and N-terminal amino-acids become discernible in the resulting products[21-23].

The latter observation suggests that intramolecular cleavage occurs during the fractionation procedure. Certain peptide bonds, particularly those involving aspartyl residues[24], are probably ruptured preferentially. Specifically, it is postulated that peptides situated near the termini of a polypeptide chain of native collagen become detached under mild experimental conditions and give rise to neutral-salt-soluble collagen. Only when native collagen is treated more vigorously will amino-acid sequences located at a greater distance from the termini of the fibre become severed to form citrate-soluble collagen plus a residual core of insoluble collagen.

It follows from the preceding considerations that differences in the metabolic turnover of various fractions of collagen should be determined by differences in the distance of the point of intramolecular cleavage from the metabolically active terminus of the fibre. Such a view would offer a reasonable explanation for the higher level of isotope incorporation and the more rapid replacement of the fraction of neutral-salt-soluble collagen as compared with other fractions, such as insoluble collagen, since the former fraction is thought to have originated from peptide sequences vicinal to the termini of the fibre, whereas the latter fraction represents the metabolically inert core of the molecule.

In view of such apparent differences in the metabolism of various collagen fractions, speculation as to size and metabolic behaviour of the fundamental repeating unit of collagen seems pertinent. On the basis of the amino-acid composition and the nature of the peptides isolated by various investigators from partial hydrolysates of collagen, it seems unlikely that molecular enlargement takes place by means of the addition of single amino-acid residues to the termini of the fibre in a random fashion. It appears more probable that a polypeptide, pre-formed on a template, is added to the collagen fibre, thereby enlarging the molecule. The size of such a polypeptide building block can be delimited. The smallest possible size can be computed from the amino-acid composition whereas the largest possible size can be estimated on the basis of metabolic data pertaining to the incorporation of amino-acids labelled with carbon-14 (refs. 1 and 2).

The residues of glycine, proline, hydroxyproline, alanine, arginine, and glutamic acid recur with unusual frequency in the peptide chains of collagen and constitute 73 moles per cent of all amino-acid residues of this protein. Aspartyl, seryl and lysyl plus hydroxylysyl residues occur in concentration of 3–6 moles per cent, whereas valyl, *iso*leucyl, phenylalanyl, methionyl and threonyl residues occur in concentrations of 1–3 moles per cent. Histidyl and tyrosyl residues occur least frequently, namely, in concentrations of 0·7–0·9 mole per cent[25]. When computed on the basis of the amino-acid occurring least frequently, the smallest building block should contain about 140 residues and should have a molecular weight of about 12,000. Alternatively, it is conceivable that under the following two conditions the amino-acid residues recurring least frequently do not determine molecular size: (*a*) residues having a low frequency of recurrence appear only as constituents of branching chains which are formed later than the peptide chain, or (*b*) these residues form the

link between two building blocks. Although the recent isolation of the tripeptide involving the ε-amino group of lysine[26] suggests the existence of such side chains, condition (*a*) appears unlikely since both amino-acid residues would have to occur in side-chains. If condition (*b*) were to prevail and the building blocks had polar and non-polar termini, these building blocks could be linked through histidyl or tyrosyl residues in two ways: (*a*) in a complementary way, that is, non-polar.polar–polar.non-polar, or (*b*) in an alternating fashion, that is, polar.non-polar–polar.non-polar. The complementary arrangement would have the advantage of accommodating readily both histidyl and tyrosyl residues so that these residues might serve in the capacity of bidentate links at the polar and non-polar termini, respectively. If these assumptions are valid, the lower limit for the size of the building block would be approximately 70 amino-acid residues and the minimal molecular weight about 6,000. Such a view is compatible with data on the composition of several polypeptides containing 20–80 amino-acid residues isolated by Grassmann *et al.*[27] as well as with the findings of Schroeder *et al.*[28], Heyns *et al.*[29] and Kroner *et al.*[30].

The upper limit for the size of the building block can be set only in terms of the ratio of the size of the building block to that of the collagen molecule. Since identical amino-acid residues in the collagen molecule are labelled non-uniformly, a ratio of about 1 : 3 for the highest to the lowest specific activity of such amino-acid residues may be considered a measure of the relative size of the fundamental building block.

The ratio of the size of the building block to that of the collagen molecule can also be computed from the ratio of the specific activities or of the turnover times of urinary 'free' and 'bound' hydroxyproline[3]. The former has a turnover time of about 0·5 day and the latter a turnover time of 15 days. The specific activity extrapolated to time zero after injection is about 50 times higher than that of bound hydroxyproline[3]. If one postulates that 'free' hydroxyproline is derived from the building blocks and 'bound' hydroxyproline from native collagen, the size of the building block may be estimated at 1/20 of the size of native collagen and would have a molecular weight of less than 3×10^5 as compared with an average molecular weight of 5×10^6 assumed for native collagen. The high specific activity in urinary 'free' hydroxyproline may also be a consequence of the unique process by which proline is hydroxylated when this amino-acid is part of a precollagenous peptide or related substances. One may postulate that the hydroxylation of proline occurs only at specific sites of the template at a time when constituents of the peptide chain are still incompletely assembled. Hydroxyproline may be assumed to have a low affinity for the template which facilitates the synthesis of the building blocks since hydroxyproline is known not to be incorporated into the nascent peptide chain of collagen and can arise only from bound proline[31–33]. Consequently, it is possible that certain hydroxyproline residues are eliminated from the template and constitute in part the source of 'free' hydroxyproline.

It is of interest to point out that an inverse relationship appears to exist in various collagen fractions between metabolic activity and carbohydrate content[10–34]. This fact may account for the differences between collagen fractions with regard to their respective solubility characteristics[35]. In spite of the low carbohydrate content of 1 per cent or less[36], the polysaccharide material may be of considerable physiological importance. One may speculate that the metabolically active terminal sites of collagen are capable of reacting with either polysaccharides or the peptide building blocks. The reaction with polysaccharides may be considered irreversible in nature and to proceed at an appreciably slower rate than the reaction with a building block, thus preventing further additions of building blocks at the sites involved. On the other hand, the reaction with building blocks is reversible and leads to enlargement or to branching of the collagen molecule. The simultaneous operation of these two reactions at the metabolically active sites of collagen would tend to restrict the process of branching and would, furthermore, provide a means of controlling the length of the peptide chain of collagen. Such a concept might be applied fruitfully to the study of metabolic inertness in relation to the process of ageing. In conclusion, it may be stated that the mechanism proposed here for the biosynthesis of collagen, although not entirely proved, suggests new avenues of approach to the study of connective tissue proteins.

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COMPARATIVE EFFECTS OF LIVER AND TUMOUR RIBONUCLEIC ACIDS ON THE NORMAL LIVER AND THE NOVIKOFF HEPATOMA CELLS OF THE RAT

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THE Novikoff hepatoma of the rat seemed to be an appropriate model to test some of the hypotheses derived from experiments with human tumour ribonucleic acid (RNA)[1–6]. It is easy to transplant, and it offers the opportunity to compare experiments with the normal counterpart organ, the liver.

RNA from normal liver and spleen and kidney from Novikoff tumour of adult (250-gm.) female Sprague–Dawley–Holtzman rats was extracted by both phenol and fluorocarbon methods[2–4,6]. 50 gm. of normal or hepatoma tissue were thrown on dry ice and extracted immediately or preserved at −20° C. for a few days. The RNA preparation was always used on the same day of preparation (less than 2 hr. at 2° C.). The ultra-violet spectra of liver RNA and hepatoma RNA show the expected difference due to the reported richness of the latter in guanine[7] (Fig. 1). The hyperchromatic effect of both RNAse and temperature indicated near-native, undenatured state.

The Novikoff tumour on the fifth day of transplantation was collected and broken in an L. Blessig manual homogenizer in phosphate-buffered saline (5 gm. of tissue in 25 ml. of salt solution). The homogenate was filtered through two layers of gauze and the cells washed four times in the RNA solvent (0·06 *M* disodium versenate, 0·06 *M* phosphate buffer *p*H 7·0, 0·12 *M* sodium chloride).

The cells are counted and then re-suspended in the RNA solution at a ratio of 2,500 µgm. RNA/10^8 cells. The suspension is left in a large bottle lying on the side to prevent cell accumulation, at 2° C. for 15 hr.

It is known that when 90 mgm. of tumour tissue are injected intraperitoneally 92 per cent of the animals have 5–8 gm. omental tumours in 5–8 days[8]. Our routine passages confirmed these data.

In one experiment 40 animals received hepatoma cells four times washed with buffered versenate–saline, and left for 15 hr. at 2° C. (group 1). Another 40 animals received hepatoma cells incubated with normal rat spleen RNA (group 2), 40 hepatoma cells incubated with kidney RNA (group 3), 40 with hepatoma cells incubated with normal rat liver RNA (group 4) and another 40 with hepatoma cells incubated with hepatoma RNA (group 5). Table 1 summarizes the results of this experiment.

Tumours in groups 4 and 5 were different from routine tumours, such as in groups 1, 2 and 3. All were considered to be modified tumours; the modifications in group 4, however, were in opposite directions from group 5.

Tumours in group 4, derived from hepatoma cells treated by normal rat liver RNA, were small (2 mm. in size) slightly hæmorrhagic nodules scattered in the mesentery, and never formed a solid omental tumour. Histologically, they showed a more orderly cordonal organization with the tendency to radiate around a vein (Fig. 3). The nucleo-cytoplasmic and nucleolo-nuclear ratios were not as markedly increased as in the routine tumour, and the cells contained glycogen in a polarized distribution, resembling normal liver. The ascitic fluid was bloody, but also contained bile elements. Mitoses were infrequent. The morphochemical characteristics, the slow growth, the low percentage of takes and the

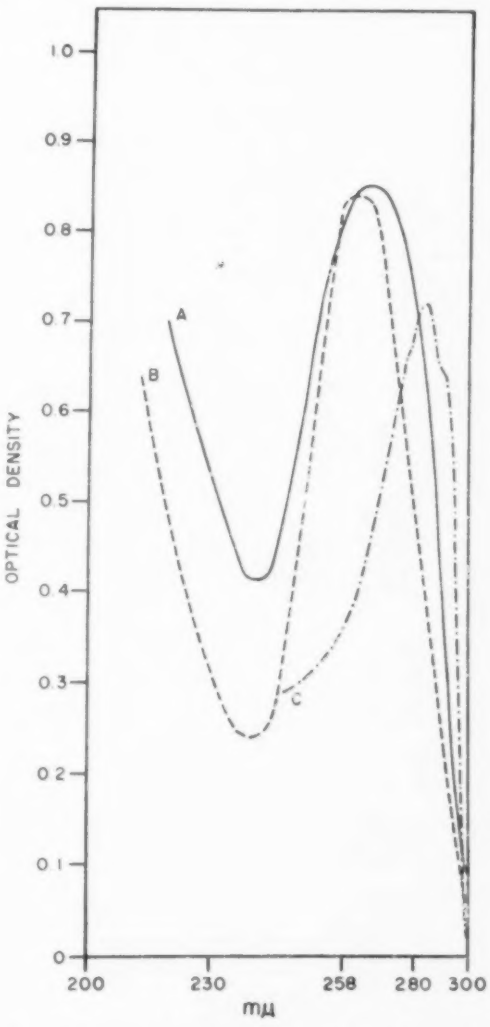

Fig. 1. Ultra-violet spectra of 10^{-5} dilution of phenol in 1/15 *M* phosphate buffer in 0·12 *M* sodium chloride, *p*H 7 at 20° C. (*C*); phenol-extracted RNA from Novikoff hepatoma (*B*); and RNA from Novikoff hepatoma modified by normal rat liver RNA (*A*)

Table 1. EFFECTS OF DIFFERENT RNA PREPARATIONS ON NOVIKOFF TUMOUR IN INTRAPERITONEAL GRAFTING

Group	RNA source	Percentage of tumours	Mean time of death (days)	Percentage of regressions
1	—	95	6	0
2	Rat spleen	94	6	0
3	Rat kidney	95	6	0
4	Rat liver	15*	12	85
5	Hepatoma	100	6	5

* Thirty-four animals still alive without tumours 95 days after inoculation. These animals were resistant to further tumour transplantations.

practical lack of lethality indicate a certain degree of re-differentiation of the original wild malignant tumour cells by the normal RNA preparation. That this action is specific to liver RNA is indicated by the fact that rat spleen and rat kidney RNA both failed to modify the tumour. These tumours were passed intraperitoneally in the usual way and did not produce the usual picture of the large malignant hæmorrhagic omental tumour in six days.

In Niu's experiments[3] Ehrlich ascites tumour cells of the mouse produced serum albumin and lost anaplastic features after treatment with liver RNA (from a mouse and a calf). It would be of interest to know whether or not they had regained malignant virulence on re-transplantation.

Since calf liver RNA in Niu's experiments was able to perform a liver-oriented differentiation (serum albumin secretion) by tumour cells, we decided to test the influence of heterologous liver RNA (rabbit) on the rat hepatoma. The following experiment was performed: eighteen rats were inoculated intraperitoneally with hepatoma cells treated by rabbit liver RNA (group 1). Six rats were inoculated with hepatoma cells treated by rabbit spleen RNA (group 2). Six rats were inoculated with hepatoma cells from the same batch used in group 1, washed in buffered saline and left for 15 hr. at 2° C.

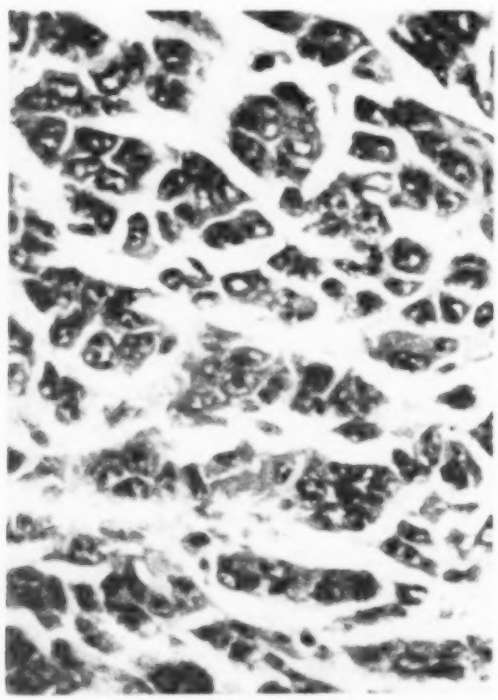

Fig. 2. Omental tumour, Novikoff hepatoma. (Histoid pattern × 275)

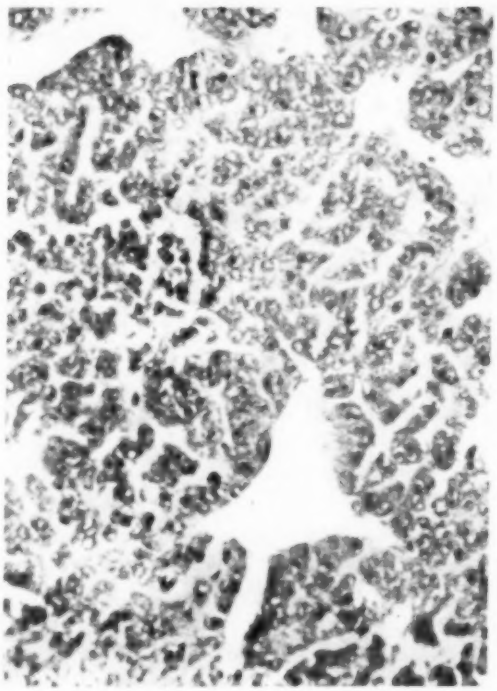

Fig. 3. Mesenteric nodule from transplantation of hepatoma cells previously treated by RNA from normal rat or rabbit liver. (Organoid pattern × 175)

An important determinant in the outcome of these experiments of tumour modification by normal RNA is the proportion of number of cells per mole of RNA. Any cell that will not incorporate enough or no RNA at all could be responsible for the restoration of the wild tumour. The exact conditions were not established in these experiments. An excess of RNA was always used to circumvent these pitfalls.

The following were the results on the sixth day after the transplantations:

Group 1. No large tumours visible. No anæmia or signs of hæmorrhage; less activity. Two animals were sampled. One had a few nodules of 1–2 mm. size in the omentum which on histological examination proved to be similar to the modified organoid type of tumours obtained with normal rat liver RNA.

Group 2. All animals had large tumours anæmic and weak; two had died on the fifth day.

Group 3. Three animals died on the sixth day with large omental tumours; the three remaining all had large tumours.

This experiment and Niu's seem to indicate that RNA from the different organs has morphogenetic-differentiating and enzyme-forming capacities that transcend species barriers and are common to homonymous organs of different species. This phenomenon is parallel to the similarity of endocrine secretions in heterologous systems and may be a fortunate event since it may allow use of specific

Table 2. Effects of Different RNA Preparations on Normal Rat Liver Cells

Group	Source of RNA	Percentage of tumours	Mean time of appearance (days)	Percentage of regression
1	—	0		
2	Liver	0*		
3	Hepatoma	20	15	5

* Small fibrotic nodules were sometimes found on the surface of the liver.

Table 3. Effect of Hepatoma RNA on the Rat

Group	Route	Percentage of tumours	Mean time of appearance (days)	Percentage of regression
1	Adult intraperitoneal	30	15	0
2	Prenatal* intravenous	10	25	40
3	Neonatal subcutaneous	5	27	40

* Results refer to offspring.

ribonucleic acids of animal origin in situations of enzyme deficiencies in man.

Supravital stainings such as acridine orange of tumour cells after 15-hr. incubation with liver RNA indicate viability of the cells after such treatment. Damage is also ruled out by the lack of effect of similar RNA preparations from other organs and from the tumour itself. Treatment of hepatoma cells with hepatoma RNA resulted in a wilder modification of the tumour. Within six days the tumour showed not only the usual large omental mass but also that this would extend to the liver, diaphragm, abdominal walls, whole peritoneal cavity, ovaries, intestines and into the pleural and pericardial cavities with a peculiar involvement of the thymus and the mediastinal and axillary lymph nodes. The thoracic involvement was noticed as extreme dyspnoea and cyanosis. In spite of all its wild features, this modified tumour regressed in a larger percentage than the unmodified variety.

In another experiment 50 animals received normal rat liver cells simply washed (group 1), treated by liver RNA (group 2) and treated by hepatoma RNA (group 3). The results are shown in Table 2. Tumours in group 3 consisted of slightly haemorrhagic nodules deep-seated in the hilum and septa of the liver with scattered mural implantations. To test whether the results of the last experiments were due to a modification of the liver cells or to a direct effect of the tumour RNA this was injected intraperitoneally into adult rats, intravenously prenatal and subcutaneously neonatal. Controls consisted of normal liver RNA and buffered versenate saline (Table 3).

Of the controls injected with normal rat liver RNA, the prenatal and neonatal showed marked retardation of growth and stunting, but no tumours in the same period that the animals exposed to tumour RNA developed tumours. Eventually, the controls resumed normal growth and development while the experimental ones died of abdominal haemorrhage.

These tumours extended throughout the peritoneal cavity, but serial sectioning of the liver and of the pancreas shows areas of possible primary tumour not found usually in the commonly transplanted hepatoma. Novikoff reports that the pancreas can be infiltrated by the tumour[8]. This causes the peritoneal implantations metastases, such as in the original Novikoff primary hepatoma. Interesting is the pancreas lesion, since liver and pancreas are two embryologically related organs. No thymus, lymph node or spleen involvement nor tumours of other localities were seen in these young. The possibility of malignant changes in liver cells induced by hepatoma RNA cannot be excluded. Ngu[9] reports the formation of local tumours when normal mouse kidney cells were treated by RNA from ascites tumour cells. However, no attempt to produce this with RNA alone has been reported.

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BLOOD NUCLEASES AND INFECTIOUS VIRAL NUCLEIC ACIDS

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IT has been shown that animal viral nucleic acids can infect tissues[1–14] and that this is not blocked by antiserum against the intact virus[3,9,11]. Since nucleases in very low concentration destroy biologically active nucleic acids[15,16], an investigation of the deoxyribonuclease (DNAase)- and ribonuclease (RNAase)-levels in human blood was undertaken to decide their possible role against infectious deoxyribonucleic acid (DNA) or ribonucleic acid (RNA).

In the course of this investigation we encountered the liberation of both nucleases and their inhibitors from the cellular elements of blood as well as the formation of a DNAase inhibitor in serum. Analyses of these materials are included because they suggest explanations for changes in nuclease-levels that are otherwise difficult to understand.

Materials and Methods

Only an outline of procedures is given here. Detailed reports will appear elsewhere. Unless otherwise

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stated, all enzyme or inhibitor assays were performed at 37° C.

DNAase assay. The substrate of this enzyme was highly purified *Hemophilus influenzae* transforming DNA which can be assayed at concentrations as low as 10^{-6} µgm./ml. A concentrated solution of this DNA which confers streptomycin resistance on a susceptible strain of this organism was added to blood, blood products, or a solution of crystalline pancreatic DNAase (Worthington Biochemical Corporation, Freehold, New Jersey) dissolved in blood electrolyte solution at *p*H 7·4. The concentration of the transforming DNA in the digestion mixture was 1 µgm./ml. The blood electrolyte solution was made up following data by Bland[17] to which was added 10 µgm./ml. of crystalline bovine serum albumin (B.E.S.A.). Samples were withdrawn at intervals and assayed for residual transforming activity by the usual procedure[18]. The slope of a curve through such points was then used to get from a standard curve of an equivalent action by known concentrations of a crystalline preparation dissolved in B.E.S.A.

DNAase inhibitor (DI). DNAase inhibitor was determined by its action against a standard pancreatic DNAase solution analysed in the same manner. A dilution of the inhibitor which reduced the rate of destruction of transforming activity by 0·001 µgm./ml. crystalline DNAase in B.E.S.A. to one-half the control value was considered as containing 1 unit of DI.

RNAase assay. A concentrated solution of yeast RNA (Schwarz and Co., Mt. Vernon, New York) at *p*H 7·4 was added to blood, blood products, or solutions of crystalline pancreatic RNAase (Worthington Biochemical Corporation) in B.E.S.A., bringing the final concentration to 10 µgm./ml. At minute intervals samples were removed and the extent of digestion measured spectrophotometrically at 260 mµ on a filtrate after chilled perchloric acid precipitation of the undigested RNA. Blood-levels of RNAase were evaluated in terms of equivalent action by known concentrations of crystalline pancreatic RNAase (Worthington Biochemical Corporation).

RNAase inhibitor (RI) assay. RNAase inhibitor was assayed by its action against 0·1 µgm./ml. of crystalline RNAase. As with DNAase, the dilution of inhibitor which reduced the action of the standard enzyme solution to half its value was thought to contain 1 RI unit.

Blood, plasma and serum. Preliminary experiments, even in the absence of anticoagulants, gave variable results with whole blood, whereas consistent and otherwise similar results were obtained with the plasma. Assays were therefore made on plasma in the absence of anticoagulants, since the latter affect the DNAase. Samples were drawn freshly through silicone-coated ('Siliclad', Clay-Adams, Incorporated, 141 E. 25th St., New York 10, N.Y.) needles and syringes and introduced into chilled coated tubes; spun at 8,000 revolutions/min. for 5 min. and the nuclease-levels of the plasma evaluated immediately. Serum was prepared by allowing freshly drawn blood to incubate for 1 hr. at 37° C. after which the serum was drawn off, centrifuged when necessary and chilled or analysed immediately.

White blood cells (WBC). Blood drawn as above was centrifuged horizontally at 2,000 revolutions/min. for 10 min. The plasma was almost completely removed and used for the isolation of platelets. The WBC of the packed cell portion on standing 5–10 min. became mixed with the residual plasma. This was removed and diluted with B.E.S.A., the cells were centrifuged and, after a second washing, they were re-suspended in B.E.S.A.

Disruption of cells. Each cell-type was suspended in a volume of B.E.S.A. to bring it to the concentration-level found in the blood. Disruption was obtained in 'Lusteroid' tubes placed in a 10-kilocycle Raytheon sonic oscillator. At full power (250 watts), disruption was essentially complete in 2·5 min. for platelets; 2 min. for WBC, and 10 min. for red blood cells (RBC).

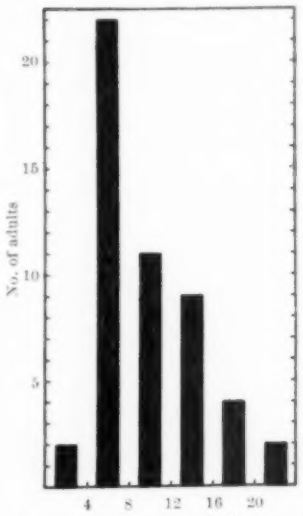

Fig. 1. DNAase-levels per ml. plasma of 50 normal adults

Experimental Results

Nuclease-levels in blood of adults. Fig. 1 shows levels of DNAase in the plasma of fifty healthy adults (25 females and 25 males). Representatives of the coloured races are included. Evidence (not shown) that the inactivation of transforming DNA is probably due to the DNAase in blood is suggested by (*a*) a quantitative correlation between destructive rate and concentration of serum, and (*b*) an independent viscosimetric analysis of serum DNAase-level. Plasma was used regularly in place of whole blood with comparable results, considering the volume difference. From Fig. 1 it appears that the range of DNAase-level in plasma of human adults is 0·0003–0·002 µgm./ml. with an average of about 0·001 µgm./ml. and half these values per ml. of whole blood. The DNAase is Type 1 (ref. 19) since it has a digestion maximum near *p*H 7.

As noted earlier[20], blood DNAase depends on divalent cations for activity; hence it is inhibited by citrate, ethylenediaminetetraacetic acid (EDTA) and other chelating agents. In the present work heparin as an anticoagulant was avoided because as little as 40 µgm./ml. inhibited plasma DNAase, yet had no apparent effect on the pancreatic depolymerase. The literature is confusing in this regard since reports indicate that heparin inhibits pancreatic DNAase[21], does not inhibit the serum enzyme[22], and that it inhibits both[23]. Some features of the system not yet understood must be critical to this reaction.

The results in Fig. 2 suggest that the level of RNAase in the blood is equivalent to approximately 0·10 ±

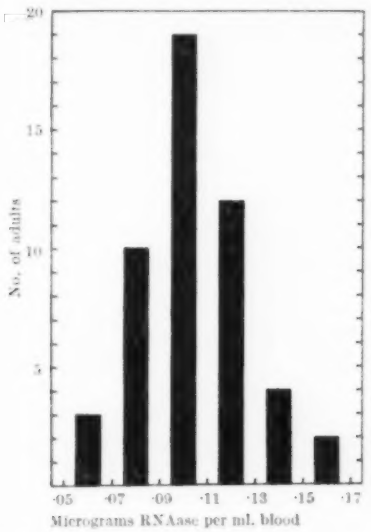

Fig. 2. DNAase-levels per ml. blood of 50 normal adults

0·05 μgm./ml. of crystalline pancreatic enzyme. Under the present conditions of study, the level of RNAase was not affected by clotting or manipulation. This result is somewhat lower than that reported earlier[2,26,27] for serum, even when correcting for the difference in volume.

Nucleases and their inhibitors in the formed elements. The DNAase activity of whole blood incubated at 37° C. decreased with time, suggesting the formation or liberation of an inhibitor. This, plus the observation that serum DNAase-levels were 2–6 times higher than the corresponding plasma-level, led to an analysis of isolated washed cellular components of blood sonically disrupted in B.E.S.A. The results are summarized in Table 1.

A sonicate of platelets contained a DNAase which could be activated by Mg^{++}. It was equivalent to 1×10^{-11} μgm. of crystalline pancreatic DNAase per platelet. These samples of blood with about 5×10^5 platelets per ml. contain 5×10^{-3} μgm./ml. DNAase, or ten times as much as found free in whole blood.

Table 1. Average Levels of Nucleases and their Inhibitors in Blood and Certain Blood Fractions

System	DNAase μgm./ml.	RNAase μgm./ml.	DNAase inhibitor units	RNAase inhibitor
Whole blood, fresh	0·0005 ± 0·0002	0·1 ± 0·05		
Plasma, fresh	0·001 ± 0·0004	0·2 ± 0·1		
Serum, fresh (from clotted whole blood)	0·006	0·2		
Serum (clotted cell-free plasma)	0·0003			
Platelets (blood concentration)	0·005			
WBC (blood concentration)	0·0	0·1	300	
RBC (blood concentration)			350	10
Serum heated at 56° C. 0·25 hr.		0·2	2	
Serum at 37° C. 15 hr.			3	
Serum + 0·01 *M* Mg^{++} 1 hr.		0·2	100	

but nearly the same concentration as found in serum from clotted blood. It seems reasonable, though not proved, that the higher serum DNAase (see Table 1) arises from disruption of platelets during clotting, for the DNAase-level of serum from clotted cell-free plasma is not higher. It is somewhat lower due, perhaps, to adsorption of the enzyme to the clot.

The presence in white blood cells of a powerful DNAase inhibitor had been known[24,25]. In the present system 1 : 300 dilution of the sonically disrupted WBC at a concentration found in whole blood, reduced the DNAase activity of a standard enzyme preparation to one-half. So, by definition, the WBC at blood-level contains 300 DI. Much of this inhibitor is released into the medium on incubation at 37° C., which may be responsible for the observed variations in enzyme-levels.

Similar sonicates of WBC contain RNAase, and it has been suggested that white blood cells are the source of serum RNAase[26].

Inhibitors of both nucleases were found in the solutions of disintegrated, washed red blood cells. Expressed in units defined in the section on Methods there were 350 DI and 10 RI per ml. of RBC at the blood level concentration.

Formation of DNAase inhibitor in serum. As noted earlier, the level of DNAase in fresh serum is several times higher than that in plasma, yet, under certain conditions, this activity is lost and it seems that an inhibitor is formed in the serum. Previous workers[20,22] had noted a loss of DNAase on heating but had offered no explanation. Since the heated serum will inhibit added pancreatic DNAase, an inhibitor for this enzyme would appear to have been formed. The conditions favouring inhibitor formation are (*a*) incubation overnight at 37° C., (*b*) incubation at 37° C. for 1–2 hr. after addition of 0·01 *M* Mg^{++}, or (*c*) heating at 56° C. for 15 min. The levels of inhibitor formed are shown in Table 1. The loss of enzymic function was not due to a loss of Mg^{++} activator, for addition of the latter brought about no restoration of activity. It is difficult to account for the difference between the present results showing formation of inhibitor at 37° C. and the reported[28] destruction of pancreatic DNAase inhibitor at 35° C.

Discussion

It seems reasonable to suppose that tissues undergoing a viral infection contain free viral nucleic acid as well as complete virus, and both these would be liberated at some stage of the infection. While complete virus can be rendered non-infectious by antibodies, the infectivity of the nucleic acid is apparently not reduced by this mechanism[3]. One wonders if the nucleic acid phase continues to spread the infection even if less effectively, or if there is another physiological defence against this phase as well.

The present work, which is confined to blood, shows that healthy human adults have nucleases which destroy biologically active nucleic acids of both types, and the question comes down to one of competing rates, that is, the rate of enzymic destruction versus the rate of infection, and the decision will be determined by the concentrations of nuclease, viral nucleic acid and the number of susceptible cells.

Work on the infectivity of viral RNA shows that normal serum destroys infectivity[1,3,6], and this destructive power is attributed to the RNAase[3]. The

present results support this conclusion, for RNAase activity is found in serum.

The rate of destruction of transforming activity by pancreatic DNAase in B.E.S.A. is about 170 logarithmic units per minute per microgram of crystalline enzyme. From results presented here, there is only 5×10^{-4} µgm. of DNAase per ml. of blood in the average healthy human being; hence, destruction will go on at the rate of about 1 logarithmic unit per 12 min., that is, 90 per cent destruction in 12 min. There is too little information on the minimum time necessary for infection in human viral diseases, especially for the naked nucleic acid phase, to draw a firm conclusion about blood DNAase as an effective defence against infectious DNA. But general considerations from work on tissue cultures[3,24] and bacterial transformations[20–22] suggest that infection of susceptible tissues by a viral nucleic acid takes place in a few minutes or less.

Schramm and Gierer[16] reported the destruction of infectivity of tobacco mosaic virus RNA by crystalline pancreatic RNAase at 8° C. Applying the usual temperature coefficient for enzyme-catalysed reactions (2 per 10 deg. C.) leads to a value for the rate of destruction at 37° C. of about 300 logarithmic units per min. per microgram of crystalline RNAase. A blood level of 0·1 µgm./ml. of RNAase would then be expected to destroy the infectivity of free RNA at the rate of 30 logarithmic units per min. per ml., or 0·5 logarithmic units per sec. Whether this is rapid enough to prevent infection is a matter for conjecture, but it is about one hundred times faster than the rate at which DNAase destroys DNA. In this connexion it should be recalled that infections are produced in animals with viral nucleic acid. Thus both RNA[4,5,7] and DNA[12] have produced infections, and in at least one case the route of infection was significant[6]. It is possible, however, that these laboratory infections developed only because relatively high levels of nucleic acid were inoculated and that the nucleases and other counteracting forces eliminate the low levels of nucleic acid that appear during the natural disease.

The experience of many virologists in completely neutralizing sera from those human beings who are ill with viral infections cannot be used as an argument against the existence of a nucleic acid phase, for the time consumed in preparing the sera and the increased DNAase-levels of serum could well militate against detection of any nucleic acid originally present in the donor's blood.

The presence of DNAase in platelets and its inhibitor in white blood cell, red blood cell and serum probably explains the wide variations in reports on blood or serum concentrations of this enzyme[20,22,24]. The RNAase in white blood cells and its inhibitor in red blood cells are not sufficient to lead to any appreciable variation in RNAase-levels in ordinary circumstances. Perhaps the wide fluctuations in DNAase-levels and its inhibitor, compared with the relatively constant level of RNAase, are due to the extremely low normal level of DNAase. The release of quite small quantities of either the enzyme or its inhibitor produces large changes in the blood level of this enzyme.

Some variations in the levels of these enzymes in the blood of sick individuals will be the subject of another communication. A few analyses of blood from individuals suffering from serum hepatitis showed no depressed levels of blood nucleases. In this anomalous disease, which prompted the present work, the long incubation and carrier periods[25] suggested a non-antigenic agent and hence, possibly, viral nucleic acid. These preliminary analyses, even if substantiated, do not exclude the possibility of a free viral nucleic acid from being important in this disease; they merely show no alteration in the nuclease-level.

An assumption, not yet tested, is involved in this work and it deserves to be mentioned. Implicit in the quantitative analysis is the assumption that the viral nucleic acids would exhibit the same response to nucleases as the arbitrarily chosen substrates. There are few data for comparison, except for experiments in which poliomyelitis RNA[3] was used. In this case, it was found that monkey serum contains RNAase equivalent to about 0·6–5 µgm./ml. of crystalline pancreatic RNAase, and species differences can be considerable[26].

Finally, it may be worth noting that the usual means of preserving blood or blood products, especially the use of chelating agents such as citrate as anticoagulant, will preserve viral DNA in an infective state by tying up the divalent cations needed for DNAase action, and methods such as heating to 60–65° C., designed to sterilize certain blood fractions, do not destroy the biological properties of DNA[27].

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Edited by R. J. C. HARRIS
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Proceedings of the Symposium held under the auspices of U.N.E.S.C.O. at Wassenaar, August 29–September 2, 1960

This international symposium was sponsored jointly by U.N.E.S.C.O., C.I.O.M.S., and the Netherlands Cancer Institute. The proceedings include not only the papers but also the major contributions to the discussion.

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Imperial Cancer Research Fund, London

Spring 1961, 431 *pp.*, *illus.*, 100*s.*

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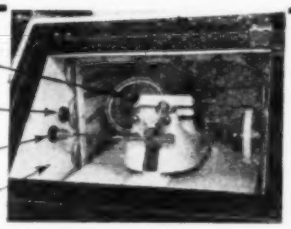

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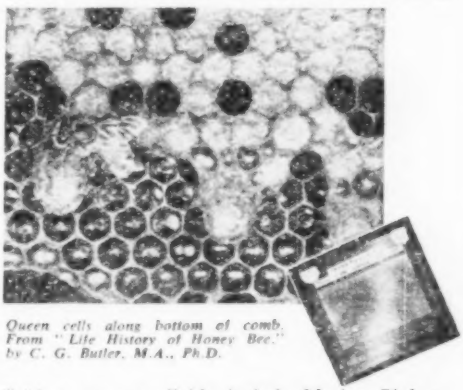

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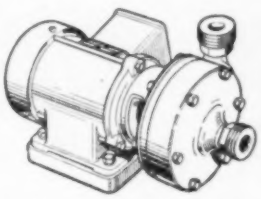

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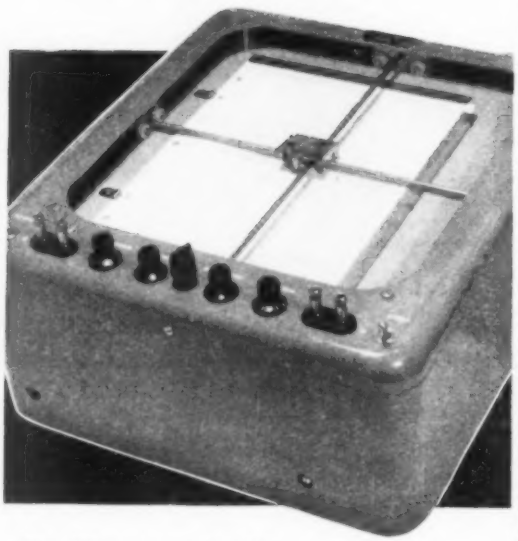

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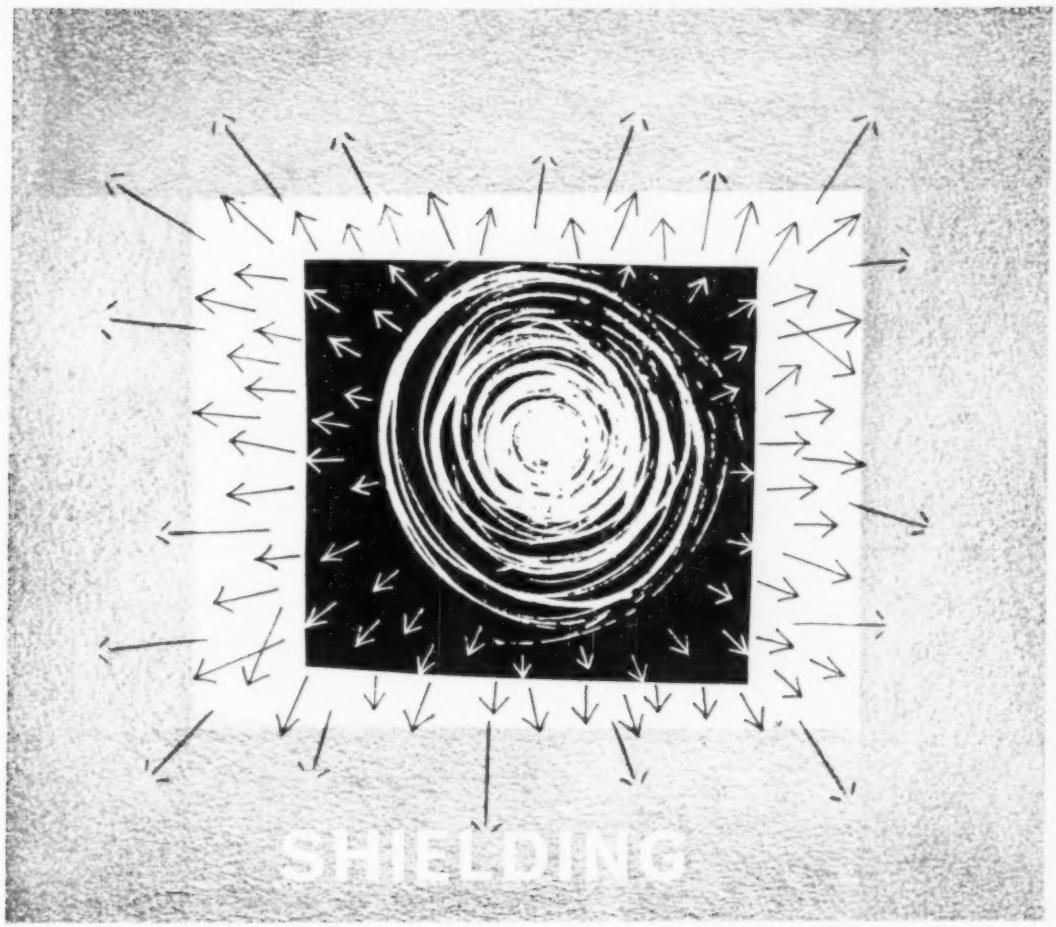

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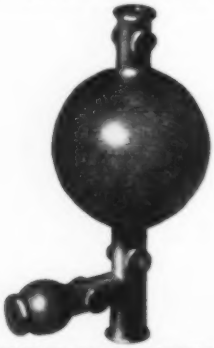

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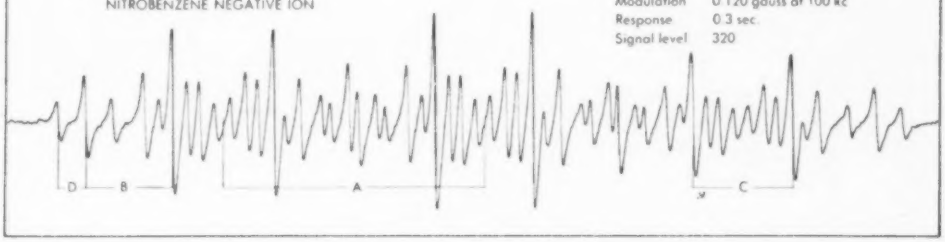

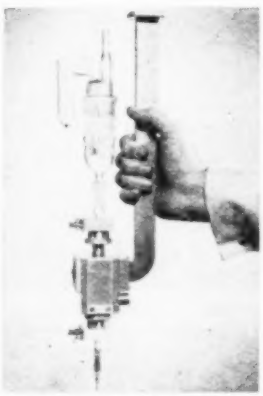

Figure 2 Electrochemical cell as used with the spectrometer

Recently Maki and Geske[1] reported a radically new and important application of EPR. They showed that it was now possible to observe directly the one electron transfer process in the electrolytic reduction of nitrobenzene to the negative ion. They prepared the negative ion by constant potential electrolysis of nitrobenzene in a solution of acetonitrile with tetra-n-propylammonium perchlorate as supporting electrolyte. Such methods of production of negative ions are preferable to the metal reduced systems in that the EPR spectrum can be interpreted completely without complication of interaction by the metal.

Figure 1 shows the spectrum of the nitrobenzene negative ion when generated from a solution of benzonitrile and tetra-n-propylammonium perchlorate[2]. Forming the ion in benzonitrile seems to improve the resolution of the spectrum obtained. The predicted 54 lines are easily observed.

Splitting (A) represents the nitrogen coupling constant which is 10.3 gauss. Splitting (B), (C) and (D) correspond to the coupling constants of the ortho, para and meta hydrogens. The electrochemical cell used in the generation of the negative ions is illustrated in Figure 2 and is a modification of the V-4548 aqueous sample cell accessory.

[1] *JACS 82, 2671 (1960).*
[2] *Sample donated by Dr. R. Adams, University of Kansas.*

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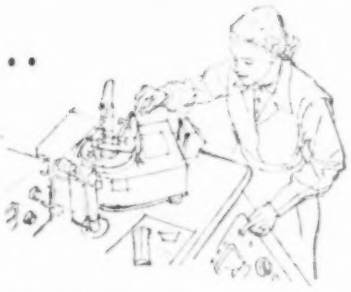

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LETTERS TO THE EDITORS

PHYSICS

The Bertele Arc

THE electron emission in the cathode spot of arcs has remained an unexplained phenomenon since K. T. Compton[1] first directed attention to it. It appears that the arc discharge discovered by H. von Bertele[2] puts this paradox into an even more acute form.

In this discharge the cathode is a polished, water-cooled thimble of molybdenum, which first must be processed in a way which suggests the formation of a very thin layer of amalgam. The molybdenum thimble is kept in contact with a small pool of mercury. The cathode spot first runs freely about on the surface of the mercury pool, but it soon becomes attached to the boundary-line between molybdenum and mercury, on which it forms what appears as a luminous line. During further processing the cathode spot gradually spreads over the molybdenum surface until it appears to cover it completely. In this operation a faintly luminous glow covers the cathode and to the eye the discharge has all the appearance of a glow discharge, while electrically it can scarcely be distinguished from an arc. The cathode drop is about 10 V., up to the highest currents which we have investigated, which were about 30 amp. on cathodes of about 1 cm.² area. The paradoxical feature of the phenomenon is the small drop in voltage, in combination with a current density which is many orders of magnitude higher than could be obtained in a glow discharge.

We have now further investigated the nature of this striking phenomenon by two lines of experiments: cinematographic observations and measurement of the current fluctuations. It was natural to suspect that the apparently steady and uniform discharge was simulated by smaller cathode-spots running about at high speed. This was in fact revealed by high-speed photographs, for which we are obliged to the Rectifier Department of the General Electric Co., Wembley. In the photographs shown, taken with an exposure of 1/15,000 sec. at intervals of 1/3,000 sec. of a cathode of about 1 cm.² area, at a current of 15 amp., the luminous glow filled at any time only about 1/10 of the cathode area. The glow has a complicated ramified appearance, and greatly changes its shape and position in intervals of 1/3,000 sec., but its area appears to remain approximately constant so long as the current is constant, and appears to increase proportionally to the current. In other words, judging from these photographs it appears that we have to do with a 'normal glow discharge', but with a current density about 150 amp./cm.² which is at least six orders higher than in the normal glow at such low pressures, though four orders lower than the current densities observed by Froome[3] in cathode spots on pool cathodes.

If this is the correct interpretation of the photographs, it appears that the cathode spot jumps rather than moves steadily from position to position, as its outlines remain remarkably sharp in photographs taken with an exposure of about 1/5 of the picture interval. It does not appear though that this violent motion is necessary for the existence of the spot. On the cylindrical mantle of the thimble one can observe in the photographs several small spots of which one has remained stationary for 1 millisecond, and in other photographs we have observed spots which were steady over periods ten times as long.

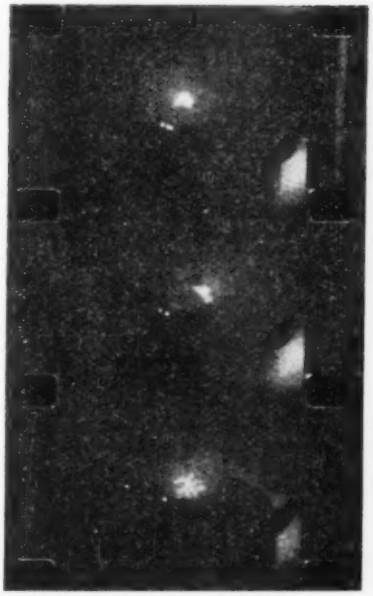

Fig. 1. Sequence of three photographs of the cathode spot in a Bertele discharge, at a picture-rate of 3,000/sec., exposure 1/15,000 sec. The cathode is a water-cooled molybdenum thimble with a blunt conical top and cylindrical shaft of 1 cm. diameter which is surrounded by an annular groove in an insulator, containing mercury during the forming, but empty during operation. Current, 15 amp.

There is, however, another possible interpretation. This is that the apparently large, diffuse spots are simulated by a number of much smaller very bright spots, running about at high speed in a restricted area, which changes from time to time. One could even assume that these spots are not essentially different from those on pool cathodes, because they are running about on a monatomic film of mercury which they rapidly evaporate. Such a hypothesis would not be absolutely contradicted by the small steady spots, because one could imagine the monatomic mercury film rapidly flowing into them from the periphery.

Unfortunately, we had no equipment available for repeating these observations at currents about 150–200 amp., at which the 'glow hypothesis' would predict that the whole surface of the cathode is permanently covered and the voltage drop would have to rise rapidly; nor could we repeat the experiment with a higher time resolution, which might have shown up the hypothetical smaller spots. We are inclined though to believe that the 'glow interpretation' is nearer to the truth, on the basis of our second

line of experiments, on the fluctuation spectrum of the arc current.

We have measured the power spectrum of the current in the frequency range from a few hundred cycles to one megacycle. In the range up to 50 kilocycles the noise-power is flat; beyond this there is a rapid fall-off with a cut-off at about one megacycle. Quantitative analysis shows that the spectrum could be accounted for by the superposition of random bursts each with the discharge of only about one million electrons. The fall-off with frequency leads to the conclusion that these bursts have a duration of certainly not less than 1 microsecond, but in most cases 10–100 times more. This is, roughly speaking, the time for which the cathode spots have been observed to be apparently steady in the high-speed photographs. The noise measurements are therefore compatible with the assumption that what we see in the photographs are real diffuse spots, steady for perhaps 0·01–0·1 millisecond. They are scarcely compatible with the explanation in terms of much smaller spots, moving about at high speeds. One could expect such small spots to cross their own path, and those of others, fairly often before the mercury film has re-established itself, and this would lead to rapid breaks in the current, which ought to have revealed itself as high-frequency noise.

The provisional conclusion from these experiments therefore appears to be that though the Bertele discharge is not an even, uniform glow, and at any time covers only a part of the cathode area, its current density is not likely to be much more than a few hundred amp./cm.^{2}, and is probably steady over times of the order of at least 10 μsec. The experiments therefore suggest that cold metal cathodes can emit electron currents of this order, with macroscopic electric fields far too small to account for field emission, without high-pressure vapour jets, and with an ion current which is probably not more than a few per cent of the electron current. We do not propose a physical explanation of this phenomenon. We only note that the observations would be compatible with elementary discharges caused each by a single ion, breaking down the barrier over an area of some 10 Å. square only, provided that an ion can linger at a distance of a few Å. before the cathode surface for several microseconds, in a sort of metastable state of high energy. There is, of course, at present no theoretical support for such a contention.

We are indebted to Dr. A. Robson, Harwell, for a critical discussion of the experiments.

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J. Vithayathil*

Department of Electrical Engineering,
Imperial College of Science and Technology,
London, S.W.1.

* Present address: Indian Institute of Science, Bangalore.

[1] Compton, K. T., *Phys. Rev.*, **21**, 266 (1923).
[2] Bertele, H. von, *Nature*, **182**, 1148 (1958); *Proc. Fourth Internat. Conf. Ionization Phenomena in Gases*, Uppsala, **1**, 359 (1959).
[3] Froome, K. D., *Proc. Phys. Soc.*, B, **62**, 805 (1949).

Diffusion of Small Molecules

The diffusion coefficient of a particle in solution is given by the Einstein equation[1]:

$$D = \frac{kT}{f} \qquad (1)$$

where f is the frictional coefficient of the diffusing substance.

For spherical and rigid particles, large compared with molecules of the solvent, Stokes found[2]:

$$f = 6\pi\eta_i r$$

By introducing this relationship into equation (1) one obtains the Einstein–Stokes equation:

$$D = \frac{kT}{6\pi\eta_i r} \qquad (2)$$

where η_i is the viscosity of the solvent, k the Boltzmann constant and r the radius of the diffusing sphere.

For spherical, but very small particles, Basset[3] has found the expression:

$$f = 6\pi\eta_i r \frac{\beta r + 2\eta_i}{\beta r + 3\eta_i}$$

where β is an empirical factor called 'coefficient of sliding friction' that ranges from zero to ∞. This introduces into equation (2) a correction factor ranging from 3/2 to 1.

Basset's equation has not yet been verified experimentally, however. Sutherland[4] carried out some diffusion measurements on alcohols and other organic substances and found that, for small molecules, the product Dr is greater than that calculated with equation (2) and decreases toward a constant value as the dimensions of the diffusing molecules increase. He considered that his measurements support the correction introduced by Basset.

This comparison is arbitrary indeed, if we consider that the model used by Stokes and Basset for their calculations is very different from a diffusing molecule, especially if it is linear instead of spherical, like alcohols and several other organic substances.

For diffusion measurements on linear and flexible molecules, we have found that, in some cases, equation (2) is verified if we substitute for r the gyration radius of the diffusing molecule to which is added the thickness of the atomic groups —CH_2— or —OH— constituting the molecule (that is, the radius corresponding to the action field of these groups). We have found that in these cases such thickness is 0·95 Å. We shall call s the sum of the gyration radius and the atomic thickness; for calculations refer to our earlier papers[5,6]. We have stated that: (*a*) when solute molecules are large compared to those of the solvent, as in the case of water solutions of organic molecules or for benzene solution of polymers, equation (2) is valid; (*b*) when solute molecules are of the same size as those of the solvent, as for benzene solutions of alcohols, esters and hydrocarbons, the radius calculated by equation (2) is smaller than the theoretical gyration radius s. The difference becomes greater when the solute and the solvent sizes are similar, and approaches zero with increasing dimensions of the solute.

Even if there is not as yet any theory relating the diffusion coefficient to the gyration radius, it is, however, interesting to note that in two cases at least, when the ratio of the dimensions of solute and solvent is great enough, equation (2) can be applied. We can, therefore, argue that a theory founded on a more realistic model should give an expression similar to equation (2).

We have used this expression to calculate the gyration radius of linear polymers in benzene, obtaining values agreeing with results using other methods[7].

In this communication we discuss some measurements carried out in the case where equation (2) is not valid, that is, when solute molecules are smaller, equal to or a little larger than those of the solvent. We have found that in this range the values of r (calculated by equation (2) from the measured values of D) are smaller than the values of s, calculated from the molecular structure.

We shall introduce the ratio s/r as a parameter to study that behaviour. Such a ratio in the case of spherical particles of Stokes's model corresponds to the correction factor calculated by Basset.

Measurements of diffusion coefficient were carried out in two solvents at 20 ± 0·01° C. by means of a method described before[6]. The precision of measurement was 0·5 per cent and the reproducibility about 1–2 per cent.

The products used were from the best firms, purified when necessary and identified by chromatographic analysis, refractive index and melting point.

The solvents were benzene and n-heptane; for the former we have assumed the value $s_{0,1} = 2{\cdot}35$ Å. (1·4 + 0·95) and for the latter $s_{0,2} = 3{\cdot}0$ Å. (2·05 + 0·95).

For the measurements in benzene see ref. 5; we list the measurements for n-heptane in Table 1.

Table 1

Substances	$D \times 10^5$ (cm.²/sec.)	r (Å.)	s (Å.)	s/r
n-Decane	206	2·50	3·50	1·40
n-Tetradecane	165	3·12	4·06	1·30
n-Octadecane	146	3·53	4·53	1·28
n-Octacosane	108	4·78	5·51	1·15
n-Dotriacontane	100	5·16	5·83	1·13
Methylcaprate	204	2·52	3·50	1·39
Methylcaproate	182	2·83	3·80	1·34
Ethyl ether	285	1·81	2·44	1·34
Dimethylketone	312	1·65	2·05	1·24

Fig. 1 shows values of s/r, measured in the two solvents, as a function of s.

We note that both behaviours are similar. In either case the values of the ratio rise to a maximum and then approach 1 asymptotically for high values of s. This confirms that equation (2) is useful for calculating the gyration radius of high molecular weight molecules like polymers with good precision, perhaps the best among the methods known nowadays. It is very interesting to point out the existence of a maximum in both cases; it was perhaps unexpected that, in a range before the maximum, smaller molecules diffuse more slowly than large ones. It is remarkable that in both cases the abscissa of the maximum is approximately the value of the gyration radius of the solvent (about 2·35 for benzene and 3 for n-heptane). A change in the rate of diffusion occurs when the solute molecules reach the dimensions of the solvent. In other words, molecules smaller than solvent molecules diffuse slower the smaller they are, while solute molecules larger than those of the solvent behave according to the Einstein–Stokes equation.

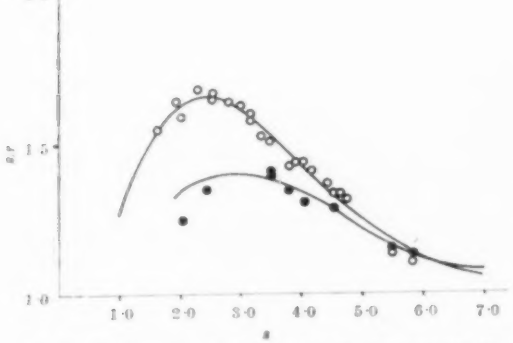

Fig. 1. ○, Measurements in benzene; ●, measurements in n-heptane

These facts are certainly related to the structure of the liquid state and to the diffusion mechanism. Therefore we think that our measurements and results can provide an interesting basis for theoretical work.

It would be useful to extend the measurements to a greater number of solvents and solutes, but, for the moment, we have limited our studies to the above cases owing to the difficulty of finding proper solvents and solutes.

We have also tried to find an empirical relation which predicts experimental results. In previous work[5] we have written an equation, very easy to apply, which accounts only for the latter part of the curve for benzene solutions and was therefore insufficient from a general point of view.

The distribution of the points and the presence of a maximum make us foresee an exponential behaviour. By trial we have found the relations:

$$s/r = 1 + 0{\cdot}90\, s^3 \exp(-1{\cdot}23s) \quad \text{for benzene}$$

$$s/r = 1 + 0{\cdot}33\, s^3 \exp(-1{\cdot}04s) \quad \text{for } n\text{-heptane}$$

which are shown as full lines in Fig. 1. As we see, they agree sufficiently with experimental values.

We have tried to formulate a single expression which includes these relationships by using as a parameter the dimension s_0 of the solvent molecules.

The two relationships may be written in the general way:

$$s/r = 1 + A_1\, s^3 \exp(-B_1 s)$$
$$s/r = 1 + A_2\, s^3 \exp(-B_2 s)$$

We have to examine whether there is a relationship between the two constants A_1 and B_1 of benzene, A_2 and B_2 of n-heptane and the dimension s_0 of the solvent molecules.

We have found that we can write:

$$A = A_1 s_{0,1}^4 = 27{\cdot}4 \qquad B = B_1 s_{0,1} = 2{\cdot}89$$

$$A = A_2 s_{0,2}^4 = 26{\cdot}7 \qquad B = B_2 s_{0,2} = 3{\cdot}12$$

The two values of A and the two of B are so close as to be considered two constants independent of s_0. This agreement is satisfactory if we take into account that the values found depend on precision of measurement of the diffusion coefficient and on the theoretical calculation of the gyration radius.

We can therefore suggest a parametric relation:

$$s/r = 1 + (A/s_0^4)s^3 \exp(-B/s_0)s$$

where A has a value of about 27 and B a value of about 3.

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Anomalous Conductivity and Lorenz Parameter in Dilute Silver-Manganese Alloys at Low Temperatures

Low-temperature electrical resistivity measurements by Gerritsen and Linde[1] on silver alloys containing small amounts of manganese in solid solution showed that, instead of attaining a temperature-independent 'residual' resistivity, they presented a minimum somewhat below liquid-hydrogen temperatures, followed by a maximum at still lower temperatures.

Measurements of the thermal conductivity (λ) of three dilute silver–manganese rods containing respectively 0·55, 0·32 and 0·14 atoms per cent of manganese revealed[2,3] an anomalous behaviour at liquid-helium temperatures in a zero magnetic field. This anomaly consisted in the $\lambda : T$ curve exhibiting a 'knee' at about 2·7° K., so that the values of λ below the knee were higher than would result if the curve above the knee were simply extended to the lower temperatures. The $\lambda/T : T$ curve exhibited this anomaly in the form of a 'dip' followed by a 'hump' at the lowest temperatures[2,4].

Since the shape of the $\lambda : T$ curve was not significantly altered by magnetic fields as high as 25 kilogauss, it was suggested that the zero-field thermal conductivity anomaly might be due to an extra contribution to the lattice thermal conductivity, owing probably to a partial uncoupling of the longitudinal and transverse phonons[2,5]. However, it was not understood why the $\lambda/T : T$ curves 'dipped' below the normal rectilinear behaviour, at temperatures between about 2·5 and 5° K. (Fig. 2, in ref. 4).

It has now been possible to analyse the thermal and electrical conductivity data on these alloys, in magnetic fields and in zero field, by the method of Grueisen–de Haas[6]. The plots of $\lambda_{[H]} : \sigma_{[H]}T$ at any temperature (where $\lambda_{[H]}$ and $\sigma_{[H]}$ are the values of the thermal and electrical conductivities for different values of the transverse magnetic field H, including $H = 0$) can be considered as straight lines. This means that the electronic Lorenz parameter L_e seems to be independent of the magnetic field-strength. However, it exhibits also an interesting variation with temperature. It is found that, in these alloys, at liquid-helium temperatures: (1) L_e is less than the 'normal' Sommerfeld value (2·45 × 10^{-8} watt-ohms-deg.$^{-2}$), but approaches that value at about 1° K. or lower; (2) L_e has a minimum value at a temperature $T_{min.}$; (3) $T_{min.}$ varies with the manganese content c, shifting to a higher temperature with increasing c, and (4) the depth of the minimum is reduced with increase of c.

The fact that L_e is less than the Sommerfeld value at liquid-helium temperatures accounts for the 'dip' in the $\lambda/T : T$ curves for these alloys, between about 2·5 and 5° K.

Full details will be published elsewhere.

Grateful acknowledgment is made of the benefit of discussions with the director, Sir K. S. Krishnan.

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Aggregation and Dispersal of Radiation Damage in Graphite

Following pioneering work by Crenall[1], Williamson[2] has used the technique of transmission electron microscopy to elucidate some aspects of the behaviour of dislocations in natural crystals of graphite, and Amelinckx and Delavignette[3] have demonstrated the formation of vacancy loops in quenched material. We have repeated some of these observations and applied the method to the study of neutron irradiation damage and its behaviour in crystals annealed up to 2,500° C. Our results appear to be consistent with those of Bollmann[4], who obtained photographs of defects in artificial graphite annealed up to 400° C.

Crystals of natural graphite obtained from Ticonderoga calcite were irradiated in the high-flux reactors *Dido* and *Pluto* to doses of about 4·8 × 10^{20} neutrons per sq. cm. (~500 equivalent megawatt-days per tonne (of fuel)) at various temperatures in the range 150–650° C. It was found advisable to give the crystals a purifying heat treatment at 1,500° C. before irradiation. Even then, however, the unirradiated material showed some flaws, including lenticular formations with diameters in the range 0·1–3μ similar to those first seen by Rang[5] in mica. Specimens were prepared by repeated cleavage using adhesive tape, and were examined in a Siemens Elmiskop microscope at 100-kV. anode voltage.

The general behaviour of the damage effects seen is illustrated in Figs. 1 and 2, which are on a scale of 120,000 : 1. The material of Fig. 1*a* was irradiated at 200° C. and the damage is present as very fine speckling, barely resolved but quite clear in the neighbourhood of an extinction contour. The light and dark contrast is of no particular significance, as the same feature changes from one to the other when the contour is moved by tilting the specimen. At higher temperatures, damage sites are larger, rounder and more sparse, as illustrated in Fig. 1*b*, which was obtained by irradiation at 650° C. Dislocations have not been found on material irradiated at the lower temperatures and are difficult to see on material irradiated at the higher temperatures. Dark-field images show no additional features.

Annealing of the low-temperature damage causes the defects to form clusters, the effect becoming marked at about 1,000° C. as shown in Fig. 1*c*. The clusters

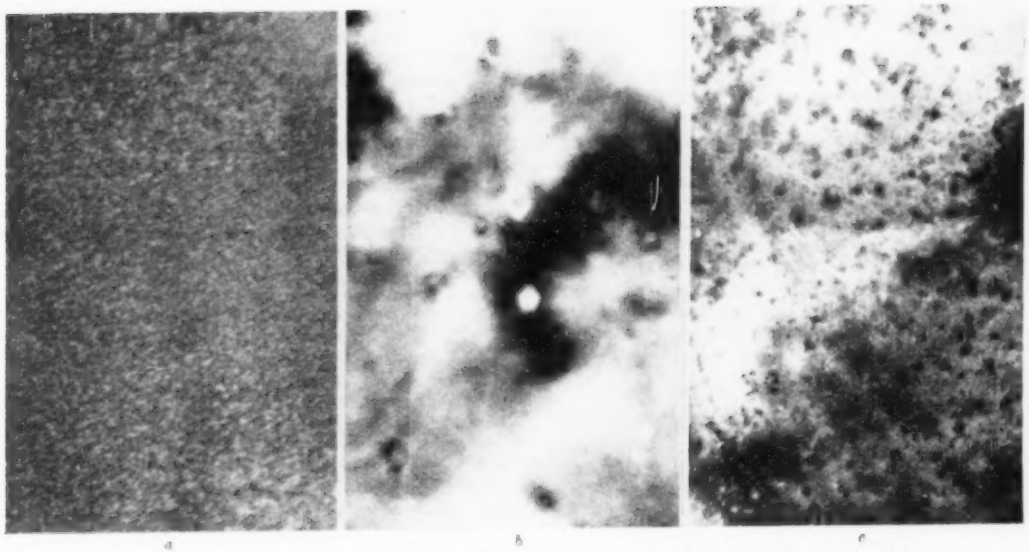

Fig. 1. *a*, Irradiation at 200° C.; *b*, irradiation at 650° C.; *c*, irradiation at 200° C. and annealing at 1,000° C.

appear to be very complex, and they are very irregular in shape, each one being apparently made up of a number of smaller units which are probably in different planes. It is possible that these clusters are formed by the migrations of smaller groups, but more likely that they are formed by the preferential growth of some sites as the less-stable ones break up. The process continues up to 1,500° C., as illustrated by the large clusters in Fig. 2*a*. Sometimes these large clusters align themselves in particular directions, as shown in Fig. 2*b*; but these directions have not been found to correspond to any particular crystal lattice vector as tested by the local electron diffraction pattern. They are therefore assumed to be associated with a local dislocation array. A few examples have also been found of alignment on parallel smooth curves. In other regions, the clusters spread out roughly along the hexagonal sides of a 'chicken-wire' pattern, as in Fig. 2*c*, suggesting that possibly ascertainable fields of force exist between complexes.

Damage incurred at 150° C. begins to disappear rapidly at annealing temperatures above 1,500° C. At 1,550° C., many of the larger clusters have been broken up, and at 1,700° C. there is little evidence of damage except a possibly enhanced dislocation density. Specimens annealed at higher temperatures are indistinguishable from unirradiated material, but there is some evidence that material irradiated at 200° C. requires slightly higher temperatures for complete annealing.

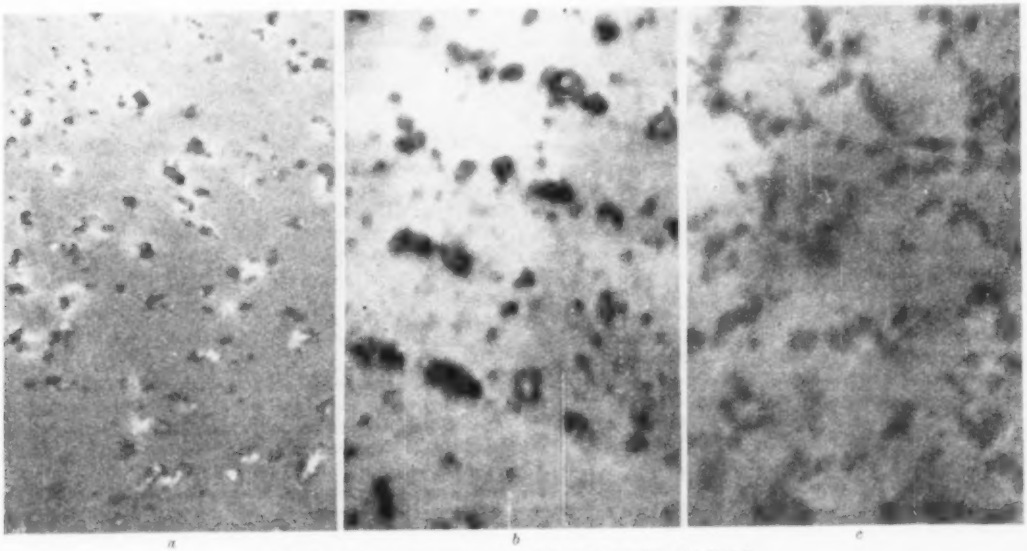

Fig. 2. *a*, *b* and *c*, Irradiation at 200° C. and annealing at 1,500° C.

It is not yet possible to say definitely whether the damage seen is predominantly due to interstitial atoms or vacancies, or if both kinds of defect are involved. However, interstitials are thought to be more mobile at least up to 1,000° C., and the general behaviour does not seem to correspond to that of vacancies as described by Amelinckx and Delavignette[5], so that it may be assumed provisionally that the effects constitute a direct observation of the behaviour of interstitial clusters.

General studies of neutron-irradiated graphite (see, for example, Simmons[6]) have already suggested the formation of highly stable complexes by the annealing of low-temperature damage, and more detailed studies will now be possible. The rapid disappearance of defects above 1,500° C. corresponds well with the final annealing of electrical effects observed in unpublished work by Eatherly.

We wish to thank Messrs. J. H. W. Simmons and R. S. Barnes for their interest and encouragement.

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GEOPHYSICS

Auroral Observations at Halley Bay, Antarctica, during 1959

In accordance with the recommendations of the Special Committee on Antarctic Research the programme of auroral observation conducted during the International Geophysical Year at Halley Bay, Antarctica, was continued into 1959. The Halley Bay Base, established by the Royal Society International Geophysical Year Expedition and now administered by the Falkland Islands Dependencies Survey, is situated in geomagnetic latitude 66° S., and both visual and all-sky camera records are now available for the four years 1956–59. A detailed analysis of the results of the first three years observations has appeared elsewhere[1], and it is interesting to compare these results with those obtained during 1959.

Of particular interest is the apparent change in the position of the southern auroral zone over the course of the four years which includes the period of sunspot maximum in 1957. Previously[2] the position of a 'quiet arc zone' has been defined in terms of the median value and interquartile range of the latitudinal distribution of quiet arcs. Such a distribution has now been obtained using the results of the 1959 observations; the positions of the quiet arc zone for the four consecutive years are given in Table 1.

Table 1

Year	1956	1957	1958	1959
Median latitude (°S. geomagnetic)	70·8	71·8	71·9	71·0
Interquartile range	±1·3	±1·0	±1·0	±1·1

Paton[3] has recently suggested that there may be a simple geometrical connexion between the position of the quiet arc zones in the two hemispheres and the 'horns' of the Van Allen belts of geomagnetically trapped radiation. The changes in the character of these belts during the period July 1958–August 1959[4] are certainly in keeping with this proposal.

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METALLURGY

Theory of the Deformation and Fracture of Body-centred Cubic Transition Metals

Experiments on a number of body-centred cubic transition metals[1] have shown that, above the ductile–brittle transition temperature, the yield stress, σ_y, varies with the average grain diameter, $2d$, according to the relation:

$$\sigma_y = \sigma_i + k_y d^{-1/2} \qquad (1)$$

Below the transition temperature, the brittle fracture stress, σ_f, is related to the grain size by the similar relation:

$$\sigma_f = \sigma_i + k_f d^{-1/2} \qquad (2)$$

Cottrell[2] has developed a theory of the ductile–brittle transition in terms of the parameters σ_i and k_y. According to the model adopted by Cottrell, σ_i is a lattice friction stress which contains a temperature-dependent part tentatively attributed to the Peierls–Nabarro stress of the lattice. The grain size parameter, k_y, is related to the stress, σ_d, required to unpin a dislocation from its impurity atmosphere and is given by the equation:

$$k_y = \sigma_d l^{*1/2} \qquad (3)$$

where l^* is the average distance from a grain boundary to the nearest dislocation source. In developing his theory Cottrell found that for a specimen to be brittle the criterion:

$$(\sigma_i d^{1/2} + k_y) k_y \geqslant \beta \mu \gamma \qquad (4)$$

must be satisfied. Here β is a constant which is nearly unity, for uniaxial tension, μ is the rigidity modulus, and γ the effective surface energy for fracture. The relations between the brittle fracture stress, the stress for ductile cleavage fracture, $\sigma_{f'}$, and the grain size which he obtained were:

$$\sigma_f(\sigma_f - \sigma_i)d = \beta \mu \gamma \qquad (5)$$

and

$$\sigma_{f'} = \frac{\beta \mu \gamma}{k_y} \; d^{-1/2} \qquad (6)$$

These equations appeared, at the time that the theory was formulated, to agree with most of the available experimental results, although no adequate results existed to test equation (6). Equation (5) is not significantly different from equation (2) over the ranges of grain size and temperature so far studied.

Recent experimental work in this laboratory and elsewhere has revealed several inadequacies in the theory of which three will be considered. First, a

set of measurements on molybdenum at − 78° C. (ref. 3) has shown that the dependence of ductile cleavage fracture stress on grain size is not correctly described by equation (6). Secondly, it has been found that the value of k_y for niobium is very small or zero at all temperatures[1]. This suggests, from equation (3), that the dislocation locking in niobium is very weak. On the other hand, sharp yielding is observed in niobium up to about 400° C. (ref. 4), and this suggests that the locking is at least as strong as in iron. Thirdly, since k_y is proportional to the unpinning stress, it should be strain-rate sensitive, whereas a recent set of measurements on iron and steel[5] have shown that it is not.

In order to explain these discrepancies between the experimental results and Cottrell's theory, I have found it necessary to develop a modified form of the theory. This has involved a re-interpretation of the parameters σ_i and k_y. Since a full account of this theory will be published elsewhere, only an outline of the main conclusions reached will be given here.

It has been established that the parameter σ_i is the sum of two terms, $\sigma_i(\mathrm{I})$ and $\sigma_i(L)$, that is :

$$\sigma_i = \sigma_i(\mathrm{I}) + \sigma_i(L) \qquad (7)$$

where $\sigma_i(\mathrm{I})$ is a lattice friction stress due to impurities and $\sigma_i(L)$ is the stress required to propagate a Luders band through a single crystal having no lattice friction stress. The term $\sigma_i(L)$ is a function of the unpinning stress, σ_d, and of the work-hardening properties of the metal, and it is therefore strongly temperature dependent. The Peierls–Nabarro stress does not contribute significantly to σ_i. The parameter k_y is a measure of the work-hardening which occurs near grain boundaries during the propagation of a Luders band in a polycrystal. It is determined mainly by the work-hardening properties of the metal, but is also influenced by the unpinning stress, σ_d.

The treatment of brittle fracture and the ductile–brittle transition given in the theory is based on the observation that, at and above the transition temperature, a growing microcrack is unable to penetrate the region of forced slip near the boundary of the grain in which it is nucleated. The criterion for brittle-fracture is then :

$$\sigma_i + k_y l^{-1/2} + \Delta\sigma \geqslant \sqrt{\frac{2\gamma_e E}{\pi(d - d_a)}} \qquad (8)$$

Here $\Delta\sigma$ is the magnitude of the yield drop, γ_e is the effective surface energy for fracture, E is Young's modulus, and d_a is the distance from the tip of an arrested crack to the grain boundary. The values of γ_e calculated from equation (8) vary from metal to metal and for a given metal depend on grain size. They lie in the range $8{\cdot}5 \times 10^3$ to $6{\cdot}5 \times 10^5$ ergs cm.$^{-2}$.

The interpretation of these values of γ_e leads to the conclusion that for a body-centred cubic transition metal to be relatively brittle it must have both strongly locked dislocations and a high work-hardening rate. The transition temperature comes out to be roughly independent of grain size for brittle metals, such as tungsten and molybdenum, but strongly dependent on grain size for relatively ductile metals, such as niobium and steel.

The theory has also been used to reinterpret existing experimental results on the hardening and embrittlement of mild steel[6] and molybdenum[7] by neutron irradiation. It is found that, as a result of irradiating mild steel near room temperature, both the friction stress, $\sigma_i(\mathrm{I})$, and the unpinning stress, σ_d, increase. In the case of molybdenum, only σ_d increases significantly. The deviation from equation (1) shown by irradiated molybdenum is shown to be the consequence of a combination of a particularly high unpinning stress and a high work-hardening rate. The theory predicts that the increase in transition temperature caused by irradiating mild steel should be greatest in specimens having a fine grain size, and that for large neutron doses the transition temperature should become independent of grain size.

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CHEMISTRY

Electronic Properties of Phenazine

Many organic compounds such as naphthalene, anthracene, etc., have extremely small, but detectable, electrical conductivities, which increase exponentially with an increase in temperature according to the equation $\sigma = \sigma_0 \exp(-E/2kT)$, where σ is the specific resistivity, σ_0 is a constant, E is an activation energy generally referred to as the energy gap and T is the absolute temperature. Since it is generally held that the conductivity is electronic rather than ionic, these substances have been termed organic semiconductors[1]. Lyons[2] has pointed out that a correlation exists between the magnitude of the energy gap and a number of molecular properties, such as the molecular ionization energy, the molecular electron affinity, and the excitation energy of the ground-triplet state transition. If it is assumed that the semiconductivity of organic compounds involves the formation of biradicals and hence participation of the triplet state in the conduction process, it becomes evident that the energy gap should be at least equal to the ground-triplet state excitation energy. Of particular interest is the fact that for a number of compounds the energy gap is roughly equal to (generally slightly larger than) the aforementioned excitation energy. Thus, the energy gaps[2] for anthracene, naphthacene, chrysene, pyrene, and anthanthrene are, respectively, 1·95, 1·64, 2·04, 2·06, and 1·58 eV., which are in fair agreement with the ground-triplet excitation energies of 1·82[4], 1·26[5], 2·45[4], 2·08[3], and 1·32[3] eV.

We have now found that this relationship apparently also holds true for the heterocyclic compound phenazine. From the dependence on temperature of the resistivity (Fig. 1*a*) of phenazine in the range of 98–143° C., we determined the energy gap as 2·1 eV. This compares favourably with the ground-triplet excitation energy[6] of 1·9 eV. The resistivity was determined in an atmosphere of dry nitrogen on a disk of phenazine which was prepared by compaction

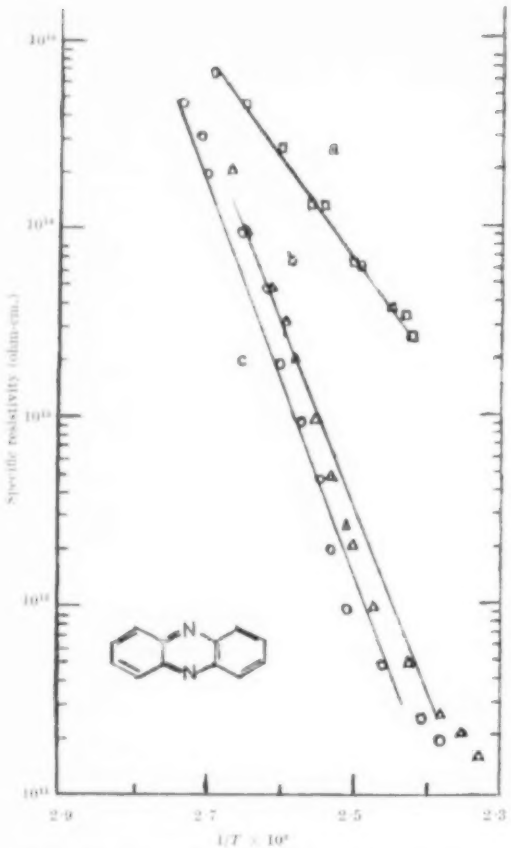

Fig. 1. Specific resistivity of phenazine: a, □, zone-refined, 94 and 940 V./cm.; b, △, two sublimations, 68 V./cm.; c, ○, three sublimations, 67 V./cm.

under high pressure and which was sandwiched between mercury electrodes during the measurements.

There is no *a priori* reason for suspecting that the energy gap obtained from measurements on a compacted polycrystalline material is different from that of a single crystal. Although the possibility of the presence of intergranular resistances in compacted specimens cannot be ruled out, these resistances should not be more serious than those possibly present in evaporated films. Northrop[3] has shown that whereas evaporated films of hydrocarbons have higher specific resistivities than single crystals, both have the same energy gap within experimental error. It is therefore apparent that reliable and theoretically significant energy gaps (albeit not specific resistivities) can be derived from measurements on suitably prepared void-free polycrystalline materials.

The phenazine was purified by chromatography on alumina and subsequent zone-refining, but estimation of the degree of purity was not attempted.

While the process of zone-refining in itself does not constitute evidence of 'hyperpurity', results obtained on conventionally purified phenazine lend support to the assumption that a specimen of high purity was on hand. Figs. 1*b* and 1*c* show, respectively, the resistivity of phenazine which, after chromatography, had been sublimed two and three times in a high vacuum. Both specimens display lower resistivities, particularly at the higher temperatures, and have energy gaps of 3·8–4·0 eV. As it is unlikely that the zone-refined specimen contained a larger number of inert impurities or physical voids than the sublimed specimens, it may be concluded that the higher specific resistivity and lower energy gap obtained in the former are consequences of its greater state of purity.

A detailed account of this work will be published elsewhere. It was supported by the Air Research and Development Command, United States Air Force, under Contract No. *AF* 33(616)–6908 monitored by the Materials Laboratory, Wright Air Development Division, Wright-Patterson Air Force Base, Ohio.

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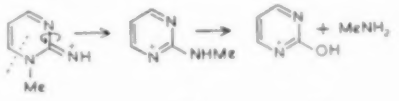
Apparent Migration of N-Methyl Groups in the Pyrimidine Series

The long-standing problem of how methyl groups migrate from nuclear to extra-nuclear nitrogen atoms in heterocyclic compounds has now been decided experimentally in the pyrimidine series.

Methyl iodide reacts[1] with 2-aminopyrimidine to give the hydroiodide of 1,2-dihydro-2-imino-1-methylpyrimidine (I). The free base may be liberated with cold sodium hydroxide, but if the alkaline solution is warmed, rearrangement to 2-methylaminopyrimidine (II) is complete in 10 min.[1,2]. Similar rearrangements are known to occur under both alkaline and acidic conditions in the pyrimidine[3–6], pyridine[7,8], pteridine[9], purine[10], and other[11,12] series.

Two facts of possible significance in connexion with the mechanism of such isomerizations are: (*a*) Rearrangement occurs only when the methyl group and the amino- or imino-group are attached to neighbouring nuclear atoms, and never when they are placed otherwise. (*b*) A nuclear-N-methylated methylaminopyrimidine failed[2] to yield a dimethylaminopyrimidine under conditions where this might reasonably be expected to happen. These facts suggest a hypothesis of hydrolytic ring fission followed by rotation and recyclization. Thus, for example, the rather polarized 1,6-bond in compound (I) would break, allowing rotation about the 2,3-bond and recyclization to the almost aromatically stable compound (II). If this hypothesis is correct, the extra-nuclear nitrogen atom in compound (I) would become a nuclear atom of compound (II).



I II III

To test the hypothesis by this means, 2-chloropyrimidine was heated with ammonia (enriched by nitrogen-15) in ethanol for 2 hr. at 120° C. to give 2-aminopyrimidine labelled in the amino group. This was treated with methyl iodide[1], and the resulting compound (I) (hydroiodide, of melting point 251° C. undepressed by admixture with unlabelled material) was rearranged[11] in hot alkali to 2-methylaminopyrimidine (II). Hydrolysis of the sublimed material (melting point 58° C.; published 59–60° C.) with *N* hydrochloric acid at 160° C. for 6 hr. gave 2-hydroxypyrimidine (III) (melting point 178° C.; published[12] 178–80° C.) and after making the residual solution alkaline, methylamine was isolated using steam-distillation and collected as its picrate (melting point 207° C., undepressed by authentic material). Mass-spectrometric examination of nitrogen samples prepared by burning compound (III) and the methylamine picrate showed a strong nitrogen-15 enrichment in nitrogen from the 2-hydroxypyrimidine, but none in nitrogen from the picrate. The rotation hypothesis for the mechanism of rearrangement was thus valid.

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The Sodium Silicate – Ferrous Hydroxide System

We have reported earlier[1] the occurrence of a point of inflexion at *p*H 10·75 on the hydrolysis curve of a 0·01 *M* sodium silicate solution which was attributed to the formation of the trihydroxy – *ortho*silicate ion, but we were unable to detect with certainty a point on this curve corresponding to the final decomposition of this ion to *ortho*silicic acid, $Si(OH)_4$. An investigation of the sodium silicate – ferrous hydroxide system has shed new light on this problem. It is known that controlled oxidation of ferrous hydroxide between *p*H 5·2 and 11·5 yields magnetite[2,3], and it has also been established[4] that silica prevents the formation of magnetite from solution. One could therefore expect a systematic investigation of the sodium silicate – ferrous hydroxide system over a wide *p*H range to assist in clarifying the behaviour of silicic acid.

The experimental procedure involved addition of sodium silicate solutions to 0·005 *M* suspension of precipitated ferrous hydroxide, yielding a final ratio of sodium silicate to ferrous hydroxide of 0·4 : 1 (excess ferrous hydroxide) and 1·5 : 1 (excess silicate) respectively, and subsequent oxidation of two-thirds of the iron present with 0·3 per cent hydrogen peroxide; *p*H of the mixture was varied between 5·1 and 13·8 and the entire operation carried out under a nitrogen atmosphere at 25 ± 0·02° C. Samples were tested for magnetic behaviour and submitted to X-ray analysis using the powder diffraction method.

We found that, below about *p*H 10·7, magnetite is not formed in any appreciable quantities, whereas above this point it is the major product together with some very finely divided γ-ferric oxide. On the other hand, an analogous procedure in the absence of silicate ions led us to establish *p*H 5·25 as the lower limit for the formation of magnetite.

It would therefore appear that *p*H 10·7 marks the end of hydrolysis of the dihydroxy – *ortho*silicate ion in 0·002–0·007 *M* sodium silicate solutions:

$$(SiO_2(OH)_2)^{2-} + 2H_2O = Si(OH)_4 + 2OH^-$$

Such freshly formed silicic acid in aqueous solution, being in an active condition[5], will be readily adsorbed by ferrous hydroxide particles and thus prevent the formation of magnetite below *p*H 10·7. This finding can be related to a recent observation[6] that at *p*H 8·5 the formation of magnetite from solution is a solid phase reaction.

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Reaction of Phosphorylating Agents with 2-Methyl-Δ^2-Oxazoline

Degradation of esteratic enzymes which have been inhibited with di*iso*propyl phosphorofluoridate (DFP) yields serine phosphate[1], although serine itself is completely unreactive to DFP[2]. Kinetic and other evidence[3] suggests participation of the imidazole ring of a histidine moiety in the phosphorylation reaction, although it is not known if the ring is the initial site of phosphorylation or whether it catalyses phosphorylation of the serine. Rydon[4] has postulated that a Δ^2-oxazoline is present in the enzyme which on phosphorylation yields an O-phosphoryl serine residue. This hypothesis was based on the results of Porter *et al.*[5], who showed that 2-aminoethyl phosphate could be isolated from the reaction of 2-methyl-Δ^2-oxazoline (I) and DFP in aqueous solution. Since acylating agents[6] react with I to give stable N-acyl derivatives, and since 2-aminoethyl phosphate was isolated by Porter *et al.* following acid hydrolysis of the product (conditions under which N → O migration of phosphoryl groups is known to occur[7]) the reaction

of I with phosphorylating agents was further examined.

An aqueous solution of I buffered at *p*H 8·2 with sodium bicarbonate reacted with an equimolar amount of di*iso*propyl phosphorochloridate (DCIP) to give, after stirring for 24 hr. at room temperature, di*iso*-propyl 2-acetoxyethylphosphoramidate in 51 per cent yield. Under these conditions no phosphorylated products were obtained with DFP. When the experiment was repeated with a three-fold excess of DFP under the conditions employed by Porter *et al.* (*p*H 7·8, 37°, 4 days with *iso*propanol added to homogenize the system[8]) two products were isolated from a chloroform extract by chromatography on Woelm IV neutral alumina followed by quantitative electrophoretic separation. They were identified as 2-aminoethyl di*iso*propyl phosphate (0·07 per cent) and 2-acetamidoethyl di*iso*propyl phosphate (0·08 per cent) by means of their infra-red spectra and their behaviour on paper chromatography and electrophoresis. Using these latter conditions the reaction of DCIP with I gave di*iso*propyl 2-acetoxyethyl-phosphoramidate (20 per cent) and di*iso*propyl 2-hydroxyethylphosphoramidate (0·4 per cent). It was found that I was almost completely converted to N-acetyl ethanolamine (II) after 3½ days in water/*iso*propanol buffered at *p*H 7·8 with sodium bicarbonate. It therefore seemed feasible that the O-phosphoryl products obtained from an aqueous solution of I and DFP could have resulted from the side reaction of II with DFP. Experiments did in fact show that, under identical conditions, II reacted with DFP giving 2-acetamidoethyl di*iso*propyl phosphate (0·35 per cent).

These results indicate that the O-phosphoryl derivatives obtained from aqueous solutions of I and DFP are not formed by N → O migration during the isolation procedure. However, it is difficult to explain why DFP should react with I to give an O-phosphoryl derivative although DCIP yields a stable N-phosphoryl derivative as would be expected from the analogous reaction of acylating agents. The reaction of II with DFP giving O-phosphoryl compounds may provide an explanation of the anomaly. These facts should be borne in mind while considering the hypothesis of serine being present in the active site of esteratic enzymes as an oxazoline ring.

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Enhancement of Atomic Absorption in the Flame by Organic Solvents

Atomic absorption methods for the determination of many cations have attracted much attention[1,2] lately. The techniques so far described usually involve the use of a flame for the production of a population of atoms, but the method is of wider application than emission flame photometry and seems to be free of some, though by no means all, of the inter-element effects that bedevil emission methods. The sensitivities obtained are high, especially for certain elements, for example, magnesium, zinc, but for others, particularly in specialized applications, for example, calcium in biological materials, a higher performance is desirable, and it is therefore of interest to look for ways of enhancing sensitivity. We have found that an improvement of 100–1,000 per cent (depending on the element under assay) can frequently be achieved if the test solutions are made to contain a high (> 50 per cent v/v) concentration of an organic solvent such as propanol or acetone.

Table 1 shows the effect of a variety of alcohols at several concentrations on the atomic absorption resulting from spraying a standard magnesium chloride solution containing 2·4 p.p.m. magnesium. It will be observed that the readings increase with increasing amounts of alcohol, but that the initial small additions have a proportionally greater effect. This initial effect is more marked as the chain-length increases.

Table 1

Organic solvent (per cent)	Organic solvent				
	MeOH	EtOH	PrOH	BuOH	AmOH
0	0·187	0·181	0·185	0·180	0·180
15			0·332	(8 per cent) 0·348	(2 per cent) 0·270
33	0·326	0·389	0·447		
50	0·390	0·448	0·447		
66	0·450	0·502	0·447		

Flame coal gas, 15 lb./sq. in. in air from cylinder. Slit width, 0·2 mm. Line, 2852 Å. 2·4 p.p.m. magnesium ions. Each series sprayed three times. Range of reading ± 3 per cent.

Similar results are found with other elements, and Table 2 shows the enhancement we have found, for the elements listed, in 50 per cent *iso*propanol solution. We have found this a convenient solvent to use because the enhancement reaches a plateau at this concentration of propanol or *iso*propanol, hence there is no point in exceeding it, but the flame stability was rather better with the branched-chain alcohol.

Table 2

Element sought	Line	Atomic absorption in 50 per cent *iso*propanol is enhanced by a factor of (approximately)
Ni	3414	2
Cs	8521	1·3
Ag	3281	2
Ca	4226	3
Fe	2483	8–10
Zn	2138	2

The reason for the increased sensitivity is not clear. It is not due entirely to surface tension and viscosity changes, for experiment shows that neither the spray-rate nor the spray efficiency (that is, the fraction of the spray going forward into the flame) changes by anything like the amount required to account for the enhancement, while the addition of 'Aerosol *T*', a proprietary surface-active agent, had no effect. Moreover, the effect is quantitatively different from one element to another.

It is well known that organic solvents similarly enhance emission in the flame, and this has been attributed to increases in flame temperature, which is, of course, much more important in emission than in absorption. There is also the possibility that the

production of free atoms is favoured by the change in flame chemistry brought about by the introduction of the organic solvent. This would be effective both in absorption and emission. We have therefore carried out the following experiment. The standard apparatus used for this work (Hilger *H*.700 spectrophotometer with *H*.909 atomic absorption attachment) was modified so that the burner could be fed with the mixed aerosol from two atomizers. Then: (1) an aqueous solution was sprayed; (2) a solution in 50 per cent propanol was sprayed; (3) an aqueous solution was sprayed from one atomizer and propanol from the other. Conditions were adjusted so that the amounts of test element, water, and alcohol actually entering the flame were the same in (2) and (3). The expected enhancement was found in (2) but not in (3). Since the amounts of alcohol and water entering the flame were similar in (2) and (3) it is reasonable to suppose that chemical and temperature conditions were similar. Clearly the explanation of the enhancement must be sought elsewhere. It seems possible that it is to be found in some change in the transient conditions that exist as the solvent in the droplets evaporates in the flame; but further elucidation is required. In the meantime, there is no doubt that a useful increase in sensitivity can be achieved if it is possible to work with organic solvents similar to those described. Other classes of compound show similar effects, for example, hydrocarbons, but are not recommended as they tend to cause instability of the flame.

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Isolation of L-Galactose-6-sulphate from a Seaweed Polysaccharide

Sulphated polysaccharides occur widely as major components of many seaweeds[1]. Until now, however, locating the sulphate hemi-ester groups in the polysaccharide structure has rested upon evidence from methylation data[2,3], supported in some cases by infra-red spectroscopy[4,5]. Here we report the application of the method of partial acidic hydrolysis to determine the position of sulphate residues in porphyran, the mucilage of the red seaweed *Porphyra umbilicalis*.

Our earlier work[6,7] has shown that porphyran contains residues of D-galactose, L-galactose, 6-O-methyl-D-galactose, 3,6-anhydro-L-galactose and ester sulphate respectively in the molar ratios 100 : 110 : 118 : 73 : 140. A similar polysaccharide has been isolated from *Porphyra capensis*[8]. The fact that the 3,6-anhydrogalactosidic linkages in these polysaccharides are very sensitive to hydrolysis in acid solutions[9,10] has prompted us to seek conditions under which glycosidic hydrolysis would proceed without the occurrence of any other changes in the polysaccharide structure. Degradation of the polysaccharide with 0·58 *N* sulphuric acid at 50 ± 1° C. for 10 hr. appeared to fulfil this condition. After this treatment, and neutralization with barium carbonate, the product was separated into fractions containing relatively high molecular weight and relatively low molecular weight substances. The fraction containing relatively high molecular weight products was isolated by precipitation from 90 per cent ethanol and subjected to further acid hydrolysis. Comparison of the rates of glycosidic and ester sulphate hydrolysis (Fig. 1) showed that after 5 hr., monosaccharide sulphates would be present in the hydrolysate, with very little contaminating oligosaccharides. It was calculated that about 27 per cent of the monosaccharide sulphate combined in the original polysaccharide could be recovered in this way. The sugar sulphate fraction was accordingly isolated from the hydrolysate by a combination of chromatography with thick paper[11], chromatography on a type of charcoal sufficiently active to retain sugar sulphates[12] and electrophoresis using a thick filter paper support and a volatile buffer[13]. The product, which was obtained as a syrup, was assigned the structure of L-galactose-6-sulphate on the following evidence: Equimolar quantities of galactose and sulphate were liberated on acid hydrolysis. The substance was shown to be a monosaccharide derivative by the method of Peat, Whelan and Roberts[14], and it moved as a single spot parallel to authentic D-galactose-6-sulphate on paper chromatography in a variety of solvent systems[11,15] and on paper electrophoresis. When treated with unbuffered sodium metaperiodate solution, 3·5 moles of oxidant[16] were consumed fairly rapidly, with no liberation of formaldehyde. This is identical with the behaviour of authentic D-galactose-6-sulphate[17]. Finally, the specific optical rotation $[(\alpha)_D = -47°$, sodium salt in water $c = 0{\cdot}15]$ was equal in magnitude, but opposite in sign, to the value for an authentic specimen of D-galactose-6-sulphate[11].

The fact that this 6-sulphate has been isolated as a hydrolysis product of porphyran cannot be taken as proof of its presence as a component of the original polysaccharide, unless it can be shown that sulphate ester migration has not occurred during hydrolysis. Although acyl migration of this type is well estab-

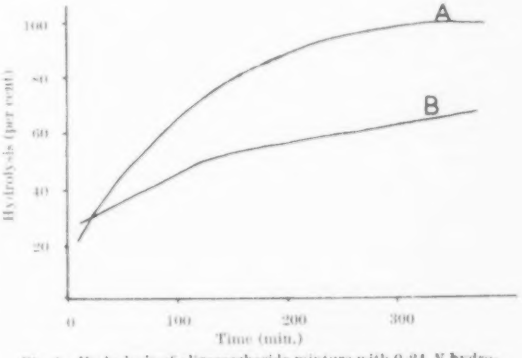

Fig. 1. Hydrolysis of oligosaccharide mixture with 0·24 *N* hydrochloric acid at 100° C. Increase in reducing power was estimated by the method of Somogyi (ref. 18) and sulphate liberation by the method of Jones and Letham (ref. 19)
A, glycosidic hydrolysis; *B*, sulphate ester hydrolysis

lished, for example, in the case of sugar acetates and sugar phosphates, it is considered unlikely here, in view of recent experiments in this laboratory with synthetic sugar sulphates. These experiments[20] have shown that when certain typical sugar sulphates (galactose-6-sulphate, galactose-4-sulphate, glucose-6-sulphate, and glucose-3-sulphate) are heated in dilute acid solution, the only reaction which can be detected by paper chromatography is the liberation of the parent sugar.

The analytical figures quoted above show that the number of sulphate ester groups present in the polysaccharide exceeds the number of L-galactose residues, and hence not all the sulphate in porphyran can occur as L-galactose-6-sulphate. Since only L-galactose-6-sulphate was isolated, it would seem that the other ester sulphates present are more acid labile. The inflexion in the curve representing the rate of sulphate release (Fig. 1) supports this view, and also suggests that more than half the total ester sulphate is liberated in the second phase of the hydrolysis at a slow rate, that is, is presumably released from the more acid-stable L-galactose 6-sulphate residues.

The conclusion is reached that L-galactose-6-sulphate is probably a major unit in the structure of porphyran. This recalls the speculations of Jones and Peat[21], to which attention has recently been directed by Hirst[1]. Jones and Peat pointed out that a simple intramolecular oxidation-reduction reaction would convert D-galactose-1-sulphate into L-galactose-6-sulphate, which could then be converted by base-catalysed sulphate elimination into 3,6-anhydro-L-galactose. Hirst has added that it is also possible to postulate a mechanism of this type for the biosynthesis of L-guluronic acid in algin.

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BIOCHEMISTRY

Localization of Arginase in Rabbit Skin

Rogers[1] has reported the induction of arginase in rabbit epithelium by the Shope papilloma virus. This conclusion was based on his findings of: (*a*) an increased uptake of arginine in papilloma tissue as compared to normal and hyperplastic whole skin; (*b*) the presence of appreciable quantities of arginase activity in papilloma tissue as compared to only trace amounts in extracts of normal skin.

We would like to propose an alternate interpretation of these findings on the basis of other data of arginase activity found in isolated tissues of the skin, interpreted in the light of the basic anatomy of the skin.

It is important to remember that the skin, exclusive of subcutaneous tissues, consists mainly of epithelium and connective tissue. The epithelial tissues (epidermis, pilosebaceous follicles, and eccrine sweat units) constitute only a relatively small fraction of whole skin, the greater bulk being connective tissue (corium). Although arginase activity is detectable in whole skin[2,3], its localization is confined to the epidermis[4–7] and epidermal appendages[8]. It is not present in the corium, at least in amounts measurable by usual methods. In pathological conditions of human skin where the epidermis is both hyperplastic and hyperkeratotic (for example, psoriasis, verruca vulgaris, plantar callus), arginase activity in the epidermis is markedly increased[5,6]. In basal cell carcinoma, however, where the epidermis is hyperplastic but not hyperkeratotic, arginase activity has been found to be normal[6]. Activity of the enzyme in skin, therefore, seems to parallel the degree of epidermal keratinization.

The present work was performed to verify that the pattern of arginase activity in rabbit skin is similar to that found in the skin of man and other animals.

The trunk skin of a normal New Zealand albino rabbit was removed and cut into half-inch strips. The strips of skin were stretched tightly on a board with dissecting needles and the epidermis scraped from the underlying corium with a scalpel[9]. The removed epidermis contained no corium, although it was visibly contaminated with hair stubble. This material was lyophilized, defatted with ether, and ground in a Wiley mill fitted with a 60-mesh screen. Only 20 mgm. of dry, powdered epidermal material was obtained from the greater portion of the trunk skin. A specimen of whole skin (containing epidermis, epidermal appendages, and corium) was powdered in similar fashion, yielding several grams of material.

Arginase activity of each tissue specimen was microassayed as described previously[9]. In this assay approximately 1-mgm. samples of epidermis, weighed on a Kahn electrobalance, were used; 5-mgm. samples of whole skin were used. The enzyme was activated by incubating the tissue with 0·2 ml. of 0·05 *M* manganese chloride at 50° C. for 1 hr. Immediately thereafter 0·05 ml. of substrate, 1·7 *M* arginine (*p*H 9·5), was added and the suspension incubated for 1 hr. at 37° C. The reaction was stopped by the addition of 0·05 ml. of 1·2 *M* sulphuric acid. The urea formed was enzymatically hydrolysed by urease at *p*H 5·0; the ammonia was liberated from solution with saturated potassium carbonate and diffused to acid in the centre well of a Conway dish. The ammonia was Nesslerized and quantitated with a Beckman *DU* spectrophotometer at a wave-length of 420 mμ. The results are shown in Table 1.

Table 1. Arginase Activity in Rabbit Skin

Experiment No.*	Wt. sample (mgm.)	γ Urea nitrogen found after enzymatic reactions			Activity†
		Complete system	Boiled tissue system	Corrected	
Epidermis					
1	0·854	53·4	14·7	38·7	4,530
2	0·982	50·1	13·6	36·5	3,715
Whole skin					
3	5·3	84·5	41·7	42·8	790

* The results of each experiment are averaged values from two or more determinations.

† Expressed as milligrams urea nitrogen per 100 gm. dry, defatted tissue resulting from hydrolysis of arginine on incubation for 1 hr. at 37° C.

The values of arginase activity obtained indicate that the enzyme in rabbit skin is largely localized in the epidermis, and that the activity in whole skin is due to the epidermis and epidermal appendages thereof. Localization of arginase in rabbit skin is thus similar to that in the skin of man. In view of the fact that arginase activity increases in hyperplastic, hyperkeratotic human epidermis, it seems reasonable to expect a similar increase in papillomas of rabbit skin, which are also characterized by epidermal hyperplasia and hyperkeratosis. The conclusion that the Shope virus induces arginase in rabbit epidermis, therefore, seems unwarranted.

The significance of arginase in normal epidermis, as well as its elevated activity in hyperkeratotic epidermis, is nevertheless unexplained. Examination of normal human epidermis for the enzymes of the Krebs–Henseleit urea cycle has revealed that, of these enzymes, only arginase is present[10]. Thus, the role of arginase in epidermis does not seem to be the same as that classically ascribed to it in liver.

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Multi-stranded Deoxyribonucleic Acid as determined by X-Irradiation

It has been widely assumed that DNA from all sources is two-stranded. However, much of the available data are consistent with more complex structures. We wish to emphasize that only those methods which actually count the number of strands per molecule are valid for examining this question. Enzyme kinetics is such a method, and has been used to show that calf thymus DNA is approximately two-stranded[1]. We have recently carried out a detailed investigation[2] of deoxyribonuclease II kinetics, using as substrates DNA samples from a variety of sources. Two classes of DNA molecules were found: namely, unitary molecules (two-stranded) and biunial molecules (four-stranded). The existence of four-stranded molecules, or pairs of double helices, has been confirmed by electron microscopy[3]. New evidence is presented here in support of these findings.

The decay in molecular weight brought about by X-irradiation has been examined as a function of X-ray dose. The following equation, which has been derived elsewhere[2], was used to express the results:

$$\frac{1-R}{R} = m(1/B)p^n = m(1/B)(kD)^n = [m(1/B)k^n](D)^n$$

where R is the ratio of the weight-average molecular weight after a given dose to the initial weight-average molecular weight; $(1-R)/R$ is the number of molecular cleavages caused by the given dose; m is the number of internucleotide bonds per polynucleotide strand; $1/B$ is a function which takes into account the possibility that molecular cleavage can occur even though the single-chain scissions are not directly opposite one another; p is the cumulative probability that a given bond will be cleaved (in the present communication, p is proportional to X-ray dose, D); n is the number of polynucleotide strands per molecule. When $\log[(1-R)/R]$ is plotted against $\log D$, as in Fig. 1, the slope of the resulting line is n.

This equation was derived for random degradation; it has been shown[2] that use of the equation when degradation is non-random leads to apparent values of n which are too low. The question is whether or not X-rays produce random degradation. It has been shown[4] that the X-ray degradation of DNA in solution is brought about indirectly by the free radicals formed in water. These occur in clusters having an initial diameter of about 20 Å. and containing about five pairs of radicals. Thus, any clusters formed in the immediate vicinity of a molecule could produce several simultaneous strand cleavages in the same region. A certain degree of non-randomness,

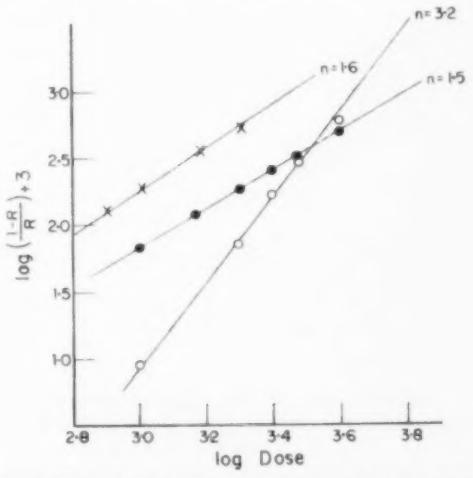

Fig. 1. Plot of log[molecular cleavages] versus log[dose], where the dose is given in rads. The slopes of the lines give values of n of 1·5, 1·6 and 3·2 for calf thymus, sea urchin sperm and *Pneumococcus* DNA respectively. The DNA samples studied have been designated as *OS*, *TS*-I and *LC*-II, respectively; their initial molecular weights were 1·9, 2·2 and 1·6 million. The isolation and disaggregation of these samples are described elsewhere (ref. 5)

resulting in low values for the number of strands per molecule, is therefore to be expected.

Molecular weights were determined by light scattering. X-irradiation was carried out with a 180-keV. source, using a copper–aluminium filter, at a rate of 80 rads/min. The concentration of DNA was 0·1 mgm./ml., in 0·002 *M* sodium acetate. Solutions were made 0·2 *M* in sodium acetate immediately after irradiation and shaken with chloroform–octanol[3] before making light-scattering measurements, which were performed within 1–2 hr. Apparently no after-effects occurred under these conditions, since there was no change in molecular weight with time (up to about 24 hr.).

Fig. 1 shows that the number of strands (n) per molecule of DNA from calf thymus, sea urchin sperm and *Pneumococcus* appears to be 1·5, 1·6 and 3·2 respectively. For calf thymus and *Pneumococcus* DNA, n was previously found[2] by deoxyribonuclease II kinetics to be 1·7 and 4·2, ± 0·3, respectively, and sea urchin sperm DNA was predicted to be two-stranded[4]. The somewhat lower values obtained in the present investigation must be attributed to non-random attacks, and thus constitute minimum estimates; the previous work was shown to involve only random enzymatic attacks. The salient point is that n for *Pneumococcus* DNA is twice that for the other samples, all of which were undenatured and had the physical properties of stiff chains or double helices. Thus, the results of the present work support the conclusions reached earlier on the basis of enzyme kinetics and other evidence, that DNA molecules from non-proliferating sources are double helices, whereas molecules from proliferating sources consist of linked pairs of double helices.

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Interference in the Diphenylamine Procedure for estimating Deoxyribonucleic Acid

The importance of deoxyribonucleic acid (DNA) in the control of cellular propagation is now well established. The amount in each somatic cell is constant for a particular species, deviations occurring with multinucleate cells or with polyploidy. With certain exceptions the DNA content of a tissue sample is directly related to the number of cells in that sample. This constancy has led to the widespread use of DNA as a standard of reference in biochemical investigations.

A general procedure for estimating DNA in tissue samples is the diphenylamine reaction; the variables of this reaction have been reviewed[1]. In most normal tissues this reaction satisfies the accepted criteria for a reliable assay method. The usual procedure is to extract the tissue with hot trichloracetic acid[2] and then to boil the extract with diphenylamine reagent for 5–15 min.; the resulting purple-blue colour is measured at 595 or 600 mμ. The extinction produced on boiling pure DNA with diphenylamine reagent increases rapidly with the time of boiling up to about 5 min., and then only slowly between 5 and 15 min.

Under certain conditions, the diphenylamine reaction is open to gross interference[1]; for example, the vivid green coloration produced by some plant extracts[3]. Dische[1] has proposed a multi-chromatic method for correcting such interference when the interfering chromagen has a sufficiently different spectrum from that of the colour produced by DNA. In general, however, such interferences are only specifically looked for when the visual appearance of the final diphenylamine colour is very different from the purple-blue of the DNA colour. The fact that interference may be considerable without appreciably affecting the visual appearance of the final colour, and the variation of such interference with time of boiling, do not appear to be sufficiently widely known.

Hot trichloracetic acid extraction of many tissues (and blood) solubilizes components other than DNA: these produce similar bluish colorations under the conditions of the diphenylamine reaction[4]. It is probable that these components are largely mucopolysaccharide in character[5]. After boiling with diphenylamine, the interfering chromagens have a main absorption maximum at 530 mμ and a smaller maximum at approximately 660 mμ (the exact position depends not only on the tissue but also on the time of boiling); these interfering colours develop more slowly on boiling with diphenylamine than is the case with DNA (ref. 4 and unpublished work). With many normal rat tissues, the amount of interference present is insufficient to produce appreciable error in estimations of DNA, providing the time of boiling is not longer than 10 min.; the extent of the interference increases rapidly with times of boiling in excess of 15 min.

With certain other tissues, however, there is considerably more interfering substance present, which produces a significant inaccuracy in estimations of DNA even when the time of boiling is 10 min. Fig. 1 shows the absorption spectra obtained by boiling a trichloracetic acid extract of involuting rat mammary gland with diphenylamine reagent for 4, 10 and 30 min. It can be seen that as the time of boiling is increased, the 530 mμ peak becomes more prominent; at the same time the extinction at 600 mμ also increases, unlike the behaviour of DNA itself. To assay DNA with any accuracy in such a tissue the time of boiling should not exceed 5 min. There is appreciably less interference present in mammary tissue at other stages in the lactation-cycle; the increased amount in involution appears to be largely the result of the accumulation of milk in the gland at this stage. The visual appearance of the final colour,

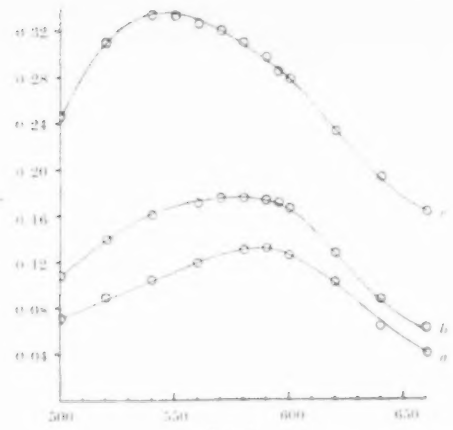

Fig. 1. Absorption spectra obtained after boiling trichloracetic acid extracts of rat mammary gland with diphenylamine reagent for varying times. Curves *a*, *b* and *c* obtained after boiling for 4, 10 and 30 min. respectively. The animal was in the first day of mammary involution, that is, the pups had been removed 24 hr. previously, at which time the rat had been in full lactation

even when considerable interference is present (as shown by a high 530-mμ peak), is not noticeably different from the colour produced by pure DNA.

Normal blood serum contains substances which interfere in the diphenylamine reaction for DNA by producing a peak at 530 mμ on boiling for long periods[3,7]. The concentration is raised in certain disease states, for example, inflammatory rheumatoid arthritis[4,5] and certain types of malignancy[7].

It is the purpose of this communication to point out that when the diphenylamine reaction is to be used for estimating DNA in tissues other than those already characterized (see refs. 1 and 2), or in which the diphenylamine reaction has been found to give results in agreement with alternative methods of assay, the variation in the absorption spectrum with time of boiling should be investigated to check the magnitude of possible interference with the time of boiling to be used. From the work on mammary gland and serum, it would appear that interference in the diphenylamine reaction can vary with the physiological status of the animal; care should therefore be exercised when using the diphenylamine reaction to compare DNA values under different physiological states when the concentration of interfering substance (mucosaccharide ?) may vary considerably.

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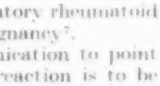
Binding of Trichloroacetic Acid by Protein

Trichloroacetic acid (TCA) is widely used as a protein coagulant in the preparation of protein-free sera; but there is little information concerning its mode of action. Rowland[1] has shown that the complete separation of protein from milk requires a concentration of 8 per cent TCA at room temperature. We have determined the amounts of TCA bound by milk proteins at this concentration (Table 1).

Table 1. Binding of Trichloroacetic Acid by Milk Proteins

Protein	No. of samples examined	Trichloroacetic acid bound: Range gm. TCA/100 gm. protein	Average gm. TCA/100 gm. protein	Average moles TCA/10^5 gm. protein
Casein	8	39–47	42	257
β-Lactoglobulin	2	92–102	97	594
Total whey protein	4	70–83	77	

In 10^5 gm. of whole casein[2] and β-lactoglobulin[2] there are 107 and 120 cationic side-chain groups respectively. If all these were available for binding TCA there remains a considerable number of sites at which the acid must be bound to account for the figures quoted above. We consider that these sites are provided by peptide bonds, the TCA being held in the following manner:



The elimination of bound water and its replacement by the strongly non-polar $Cl_3C.C$— radical destroys the solubility of the protein in water and tends to render it soluble in non-polar solvents. TCA–protein complexes dissolve to a varying degree in absolute alcohol or acetone, and the soluble fraction can be transferred to benzene and chloroform[3]. The alcohol-solubility of the TCA–protein complex varies over a narrow range for any particular undenatured protein and is related to the degree of binding of TCA by the protein (Table 2).

Table 2. Solubility in Absolute Alcohol of the Various Milk Proteins after Precipitation with TCA

Protein	No. of samples examined	Final concentration of TCA	Solubility in alcohol: Range (per cent)	Average (per cent)
Casein	14	0·5 *M*	2·87–5·38	3·95
β-Lactoglobulin	4	..	69·0–75·0	72·0
α-Lactalbumin	2	..	36·0–41·0	39·0
Globulins	1	..	10·0	10·0
Protease	1	..	9·0	9·0

In the case of TCA–casein the alcohol-solubility is unaffected by particle size and the fraction dissolved contains all the known casein fractions in approximately the same ratio as they are present in native casein. A reduction in the number of TCA binding sites reduces the alcohol-solubility of the TCA–protein, and we have used this index of solubility to follow protein denaturation, protein–protein interaction

and protein–sugar interaction in both model systems and in heated milk.

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Diglyceride Kinase and Phosphatidic Acid Phosphatase in Erythrocyte Membranes

We have recently provided evidence that in the avian salt gland sodium is pumped by a mechanism which we have termed the phosphatidic acid-cycle[1,2]. In this mechanism phosphatidate functions as a sodium ion carrier in the membrane; the phosphatidic acid-cycle consists of two enzymes—diglyceride kinase, which forms phosphatidate from diglyceride and adenosine triphosphate, and phosphatidic acid phosphatase, which hydrolyses phosphatidate to yield diglyceride and orthophosphate. If the phosphatidic acid-cycle is a general mechanism for active sodium transport one would expect to find the enzymes of this cycle in all membranes which actively pump sodium. This preliminary report is concerned with the presence of these enzymes in erythrocyte membranes.

Membranes were prepared from haemolysed human erythrocytes[3] and were incubated with an adenosine triphosphate-γ-phosphorus-32 generating system[4]. Under these conditions, phosphatidic acid became labelled with phosphorus-32; no other radioactive phosphatides were seen on chromatograms of the total lipid extracts. The radioactivity found in the phosphatidic acid spot on the chromatograms accounted for 80–100 per cent (uncorrected for breakdown of phosphatidic acid during chromatography) of the total radioactivity in the lipid extract (Table 1). These results indicate that phosphatidic acid is formed from adenosine triphosphate in the erythrocyte membrane.

Addition of diolein to the incubation system markedly increased the formation of phosphatidic acid; this indicates the presence of diglyceride kinase in the erythrocyte membrane. In the presence of added diglyceride the diglyceride kinase was stimulated by potassium, the optimum potassium concentration being 60–80 m.equiv./l. Sodium was on average about one-fifth as effective as potassium. No stimulation by sodium was observed in the presence of optimum concentrations of potassium.

Table 1. Diglyceride Kinase in Erythrocyte Membranes

Exp. No.	Cation concentration (m.equiv./l.)		Diolein added	Radioactivity in phosphatides (counts/min./mgm. dry weight of ghosts)	
	Sodium	Potassium		Total extract	Phosphatidic acid
1	60	30	0	375	298
			10 μl.	1,420	1,400
2	0	0	10 μl.	667	
	0	20	10 μl.	820	
	0	40	10 μl.	951	
	0	80	10 μl.	1,180	
	0	120	10 μl.	1,180	
	16·5	0	10 μl.	835	
	31	0	10 μl.	920	
	62	0	10 μl.	945	
	93	0	10 μl.	910	

1·2 mgm. (dry weight) of erythrocyte ghosts were incubated in 0·25 ml. of incubation medium for 1 hr. at 37° C. After incubation the radioactivity of the total lipid extract and phosphatidic acid were determined as described previously (ref. 4). The incubation medium consisted of the following (expressed as final concentrations): imidazole–histidine–*tris* buffer, *p*H 7·1 (0·025 *M*), magnesium sulphate (0·002 *M*), *tris* carbamyl phosphate-^{32}P (0·0035 *M*), dialysed carbamate kinase from *S. faecalis* (0·3 units/ml.), *tris* fluoride (0·01 *M*), *tris* adenosine diphosphate (0·0004 *M*). The specific activity of the carbamyl phosphate-^{32}P was $2·5 \times 10^6$ counts/min./μmole.

Table 2. Phosphatidic Acid Phosphatase in Erythrocyte Membranes

Exp. No.	Cations added*	Total phosphatidic acid phosphatase (mμmoles of ortho-P formed per mgm. dry wt. of ghosts)	Mg^{++}-dependent phosphatidic acid phosphatase (mμmoles of ortho-P formed per mgm. dry weight of ghosts)
1	None	5·1	
	Mg^{++}	5·1	0
	Na^+	3·1	
	$Na^+ + Mg^{++}$	9·1	6·0
	Li^+	4·9	
	$Li^+ + Mg^{++}$	9·2	4·3
	NH_4^+	4·1	
	$NH_4^+ + Mg^{++}$	6·1	2·0
	K^+	5·1	
	$K^+ + Mg^{++}$	6·2	1·1
	Cs^+	5·3	
	$Cs^+ + Mg^{++}$	5·2	0
2	None	4·6	
	Mg^{++}	9·1	4·5
	Na^+	4·0	
	$Na^+ + Mg^{++}$	13·2	9·2

* The final concentration of magnesium was 0·8 m.equiv./l. and the final concentration of each of the monovalent cations listed was 155 m.equiv./l.

5·5 mgm. (dry weight) of erythrocyte ghosts were incubated in 1·0 ml. of incubation medium at 37° C. for 1 hr. The incubation medium contained the following (expressed as final concentration): *tris* dioleyl phosphatidate-^{32}P (0·002 *M* in experiment 1 and 0·003 *M* in experiment 2) and imidazole–histidine–*tris* buffer, *p*H 7·1 (0·03 *M*). The *tris* phosphatidate ranged in specific activity from about 10 counts/min./mμmole to about 120 counts/min./mμmole. After incubation 0·05 ml. of 10 per cent crystalline bovine albumin was added to the incubation vessel, followed by 1 ml. of 10 per cent trichloracetic acid. After centrifugation the trichloracetic acid extract was washed three times with wet ether, and a 1-ml. aliquot of aqueous phase was dried on a planchet and counted. An incubation with boiled ghosts was used as the blank. All values are averages of triplicate incubations

Incubation of erythrocyte membranes with phosphatidic acid yielded orthophosphate (Table 2), indicating the presence of phosphatidic acid phosphatase. Two types of phosphatase activity were present in the membrane, one of which was independent of the presence of magnesium and one which was dependent on the presence of magnesium. The optimum concentration of magnesium was about 1 m.equiv./l. Sodium ions inhibited somewhat the magnesium-independent phosphatase but stimulated the magnesium-dependent phosphatase. In some experiments the magnesium effect was seen only in the presence of sodium, but in others a partial stimulation by magnesium occurred in the absence of sodium. Preliminary experiments indicate that the dependence of the magnesium effect on the presence of sodium develops with ageing of the preparation.

The combined actions of diglyceride kinase and phosphatidic acid phosphatase results not only in the synthesis and breakdown of phosphatidic acid but also in adenosine triphosphatase activity. Adenosine triphosphatase activity has been shown to be closely related to the action of the sodium–potassium pumps in both nerve[5] and erythrocyte[3] membranes. This adenosine triphosphatase is dependent on the presence of both sodium and potassium and also requires magnesium. Since the combined activities of the two enzymes of the phosphatidic acid-cycle require sodium, potassium and magnesium, it is possible that this cycle may be identical with the adenosine

triphosphatase activity related to the sodium–potassium pumps.

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Lecithin-splitting Enzyme of *Vibrio* El Tor

It was known that *Vibrio cholerae* and *Vibrio* El Tor excrete a lecithin-splitting enzyme in their culture medium[1–3], but the nature of this enzyme was not properly ascertained. The present communication is concerned with the characterization of the enzyme excreted by *Vibrio* El Tor with special reference to some of its important properties. The enzyme was isolated from the culture filtrate of the organism, which was grown aerobically in surface cultures using peptone–water medium for 48 hr. The culture filtrate was fractionated by ammonium sulphate and the precipitate obtained between 50–75 per cent saturation contained all the enzyme activity. This was dissolved in 0·01 *M* phosphate buffer and after dialysis against the same buffer was kept frozen at − 15° C. for about four weeks, up to which time no loss of enzyme activity has been noticed. Addition of glycerol is not necessary for its storage.

The enzyme has been found to attack only lysolecithin molecules liberating acid-soluble phosphorus and acid-labile choline compounds without any liberation of free choline and is inactive towards purified lecithin. The incubations were performed in 10-ml. stoppered centrifuge tubes into which the requisite amount of lipid substrate in chloroform solution (usually 0·75 μmole) was added. The solvent was removed *in vacuo* at about 40° C. and the lipid was then mixed up in buffer solution (50 μmoles barbital buffer of *p*H 8·0, which has been found to be its optimum *p*H). The enzyme equivalent to approximately 0·15 mgm. protein was then added and the total volume of the incubation mixture was kept 1 ml. The incubations were made at 37° C. for 1 hr., after which the reaction was stopped by the addition of trichloracetic acid solution to a final concentration of 5 per cent in the presence of bovine serum albumin (5 mgm. per flask). This was centrifuged, the centrifugate was extracted once with three volumes of a mixture of chloroform and *iso*butanol (2 : 1, v/v) and was again centrifuged. The aqueous portion which was separated was analysed for the reaction products. It has been noted that there is a decrease in the fatty acyl ester group and simultaneous increase in acid-soluble phosphorus, and these are in quantitative proportion with the release of acid-labile choline compound. This choline compound has been identified as glycerophosphoryl-choline with the help of paper chromatography according to the method described by Dawson and Rowlands[4]. The enzyme is therefore characterized as 'phospholipase *B*'.

Unlike any other phospholipase *B* from *Penicillium notatum*[5], *Aspergillus niger*[6] or from any animal tissue such as pancreas[7] and liver[8], this enzyme has a *p*H optimum of 8·0 and is fairly stable towards heat denaturation. It is destroyed only on heating at 100° C. for 15 min., and heating for 5 min. at that temperature causes about only 50 per cent inactivation. It is fairly insensitive towards metal ions, and when used at a final 1 m*M* concentration only zinc causes about 40 per cent inhibition, whereas copper, manganese, calcium and magnesium have practically no effect. Of the inhibitors studied at 10^{-3} *M* final concentration, cyanide, azaguanine and chloramphenicol have no effect, azide and dinitrophenol inhibit the enzyme to the extent of about 15–20 per cent, whereas sodium fluoride, versene and *p*-chloromercuribenzoate individually cause about 45 per cent inhibition. The inhibition by versene and by *p*-chloromercuribenzoate can be fully reversed by the addition of calcium and glutathione respectively. It has further been observed that glutathione and also cysteine bring about some stimulation of the enzyme. Work on the properties and also on the mechanism of excretion of this enzyme by both *Vibrio cholerae* and *Vibrio* El Tor is in progress.

We wish to thank Prof. B. C. Guha for his advice and interest in this work, and also Dr. R. M. C. Dawson, Cambridge, England, for his gift of a sample of glycerophosphoryl choline.

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Immunity of Bee Keepers to Some Constituents of Bee Venom : Phospholipase-*A* Antibodies

For many years bee venom has been used in the treatment of arthritis and rheumatism, but with little evidence of its value[1]. Bee venom contains three important constituents : the main toxic fraction I, and the enzyme fraction II, containing phospholipase and hyaluronidase. Each enzyme has been isolated in pure form[2,3]. The haemolytic effect of the venom on blood corpuscles is caused directly by the toxic fraction I, and indirectly by the phospholipase-*A* activity[4]. Among other effects of phospholipase-*A* is retardation of egg yolk coagulation[5].

Antibodies against the toxic fraction have not been found ; those against the enzymatic part of the venom have been demonstrated in the sera of mammals injected with bee venom for a long time[6,7]. We have therefore examined the sera of bee keepers to ascertain whether they contain antiphospholipase bodies.

Samples of blood from bee keepers were taken as test samples, and from ordinary men as control samples. The blood was left to clot at room tem-

perature, then placed in a refrigerator overnight. Serum, obtained by centrifuging and decanting, was kept in a refrigerator until required. Natural bee venom was dissolved in physiological saline (0·85 per cent) in concentrations of 1 : 1,000, 1 : 2,000 and so on up to 1 : 64,000.

To 0·05 ml. bee keeper serum were added 0·05 ml. venom solution and, after at least 15 min. at room temperature, 2 ml. of egg yolk diluted with physiological saline in the proportion of 4 : 6. The mixture was shaken, heated for 1 hr. in a water-bath at 37° C., and the tubes then plunged into boiling water and the time of coagulation recorded with a stop watch. The emulsion was considered to coagulate when no traces of the egg yolk adhere to a thick glass rod inserted repeatedly into the tubes containing the mixture. Two control experiments were carried out in the same way, one with normal serum and the other with saline instead of serum.

The methods of calculation were as follows:

Venom end concentration: 0·05 ml. venom was added to 0·05 ml. serum and 2·0 ml. egg yolk; the final dilution was 0·05 : 2·1 = 1 : 42. When original venom concentration is 1 : 2,000, the end concentration is 1 : 84,000.

Serum end concentration: 0·05 ml. serum was added to 0·05 ml. venom and 2·0 ml. egg yolk; the final dilution was 0·05 : 2·1 = 1 : 42. Serum itself was used without original dilution, therefore its end concentration is the same as the final dilution = 1 : 42.

Serum in ml. : Venom in gm.: 1 : 42/1 : 84,000 = 2,000 : 1.

Effect of serum of normal men: This is considered as activity if the time of coagulation is more prolonged, and as inhibition if time is shorter, than time of control; for example, average control saline = 24·8, average control serum of normal men = 26·3; effect of normal serum $= \frac{26{\cdot}3 - 24{\cdot}8}{24{\cdot}8} \times 100$ = 6 per cent activation.

Effect of serum of bee keepers: The effect was related to the effect of serum of normal men; for example, average control serum of normal men = 26·3, average test serum of bee keepers = 21·6; effect of bee keepers serum $= \frac{26{\cdot}3 - 21{\cdot}6}{26{\cdot}3} \times 100 = 18$ per cent inhibition.

The results obtained in a series of experiments are summarized in Table 1.

The above figures represent the averages for 4 saline controls, 6 normal sera controls and 10 bee keepers sera.

From Tables 1 and 2, it is clear that normal serum has no antiphospholipase effect against high final concentration of venom (1 : 2,000, 1 : 4,000 or 1 : 8,000). In the first two concentrations the activity of the enzyme was increased. Serum from bee keepers showed an inhibitory effect on the enzyme at previous concentrations; it reached more than 40 per cent in concentrations of 1 gm. venom to 4 litres serum.

Table 2 shows that phospholipase-*A* of bee venom was activated by serum of normal men when the concentration of the latter to that of venom was 2,000 : 4,000 : 1, and 8,000 : 1. Very dilute concentrations of 16,000 : 1 were inhibited by normal serum. Serum of bee keepers inhibited the phospholipase-*A* effect in all concentrations used.

In low concentrations of venom, such as 1 : 16,000, both normal serum and bee keepers' serum showed an inhibition of phospholipase-*A*; the latter being about 10 per cent more inhibitory.

Table 1. Effect of sera from bee keepers and control on the coagulation-time of egg-yolk

	Venom original concentration	Control saline	Control serum	Test serum
	1 : 2,000			
Mean coagulation time (min.)		24·8	26·3	21·6
Standard error of mean		4·28	4·88	4·56
	1 : 4,000			
Mean coagulation time (min.)		9·8	10·1	9·7
Standard error of mean		0·4	0·26	0·88
	1 : 8,000			
Mean coagulation time (min.)		4·8	4·9	5·0
Standard error of mean		0·57	0·30	0·41
	1 : 16,000			
Mean coagulation time (min.)		2·7	2·0	1·7
Standard error of mean		0·41	0·28	0·16

Table 2. Quantitative comparison of inhibition of phospholipase-*A* activity by sera of normal men and bee keepers

Venom end concentration	Serum end concentration	Serum : Venom (ml. : gm.)	Effect of serum of normal men	Effect of serum of bee keepers
1 : 84,000	1 : 42	2,000 : 1	activation, 6 per cent	inhibition, 18 per cent
1 : 168,000	1 : 42	4,000 : 1	activation, 3 per cent	inhibition, 4 per cent
1 : 336,000	1 : 42	8,000 : 1	activation, 2 per cent	inhibition, 39 per cent
1 : 672,000	1 : 42	16,000 : 1	inhibition, 25 per cent	inhibition, 15 per cent

We thank the Council for Combined Units for facilities in obtaining blood samples from bee keepers working in its apiaries; Dr. K. A. Forster, for providing carefully dried bee venom prepared by Mack Company, Illertissen, Germany; Blood Bank of Ain Shams University, for samples of normal blood of different blood groups; and Dr. M. Shabrawi for useful help.

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PHYSIOLOGY

Effect of Urinary *p*H on 5-Hydroxytryptamine Excretion in the Rat

Urinary *p*H influences the excretion-rate of some weak acids and bases[1,2], a more rapid excretion of weak acids occurring in alkaline urine and of weak bases in acid urine. Most of the known compounds which behave in this way are not found naturally

Table 1. Showing Urinary Excretion of 5-Hydroxytryptamine and 5-Hydroxyindoleacetic Acid as Percentage of Dose of L-^{14}C-5-Hydroxytryptophan or ^{14}C-5-Hydroxytryptamine in 'Acid' or 'Alkaline' Rats

DL-^{14}C-5-Hydroxytryptophan administration																
	Exp. 1				Exp. 2				Exp. 3				Exp. 4			
Hr. of exp.	Alkaline		Acid		Alkaline		Acid		Alkaline		Acid		Alkaline		Acid	
	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA
1	0·05	0·2	0·3	0·1	0	0	1·6	0	0·25	0	0·05	0·05	1·6	0·05	3·05	0·2
2	0·3	0·3	0·6	0·05	0·6	0·4	3·2	0·2	0·2	0·05	1·3	0·4	1·4	0·4	2·4	0·25
3					0·6	0·2	1·6	0·05	0·1	1·0	0·4	1·4	1·6	0·4	0·8	0·2
4									0·05	2·0	0·05	0·6	0·9	0·2	0·5	0
5													0·9	0	0·3	0
6																
Total (per cent)	0·35	0·5	0·9	0·15	1·2	0·6	6·4	0·25	0·6	3·05	1·8	2·45	6·4	1·05	7·05	0·65

DL-^{14}C-5-Hydroxytryptophan administration					^{14}C-5-Hydroxytryptamine administration											
	Exp. 5				Exp. 6				Exp. 7				Exp. 8			
Hr. of exp.	Alkaline		Acid		Alkaline		Acid		Alkaline		Acid		Alkaline		Acid	
	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA	5HT	5HIAA
1	3·0	0·55	2·1	0·4	0·05	0·2	0·2	0	0·2	0·35	0·2	0·75	0·85	0·9	0·65	0·35
2	2·7	4·8	4·2	0·8	0·2	0·7	0·15	0·35	0·05	0·6	0·1	1·1	0·4	2·85	1·3	7·15
3	2·2	1·8	4·2	0·6	0·05	4·2	0·1	2·4	0·05	0·7	0·1	0·5	0·3	1·45	0·7	2·1
4	1·5	0·6	1·85	0·4	0	3·5	0·1	0·35	0	0·25	0·05	0·2				
5	1·05	0·5	1·1	0·4	0	0·8	0	0·1	0	0·4	0·05	0·2				
6	0·3	0·2	0·45	0·5												
Total (per cent)	10·75	8·45	13·9	3·1	0·3	9·4	0·55	3·2	0·3	2·3	0·5	2·75	1·55	5·2	2·65	9·6

Female white Wistar rats of 200–250 gm. body-weight were depleted of sodium chloride by the dietary method of Milne *et al.*[5]. Two rats, matched for weight, were used in each experiment. One was injected intraperitoneally with 10 ml. isotonic sodium sulphate ('acid rat' – urine *p*H 5·5–6·0 throughout experimental period) and the other with 10 ml. isotonic sodium bicarbonate containing 10 mgm. acetazolamide ('alkaline rat' – urine *p*H 8·0–8·5 throughout experimental period). The injection solutions also contained 30 mgm. per kgm. body-weight of β-phenylisopropylhydrazine ('Cavodil'). One hr. later an indwelling catheter was placed in position under pentobarbitone–ether anæsthesia which was continued throughout the experiment. After 1·5 μc. DL-^{14}C-5-hydroxytryptophan (exps. 1–5) or 1·5 μc. ^{14}C-5-hydroxytryptamine (exps. 6–8) had been injected intraperitoneally, hourly collections of urine were made. Bladder washings of 3 × 1 ml. isotonic sodium chloride, obtained at the end of each hour, were added to urine excreted during that hour.

Specimens of urine were analysed for total number of counts and portions were also extracted (refs. 5, 6) and assayed for ^{14}C-labelled 5-hydroxytryptamine or 5-hydroxyindoleacetic acid using a thin end-window Geiger counter.

in the body. The only endogenous substances so far described, the excretion-rate of which is dependent on urinary *p*H, are ammonia[3] and indoleacetic acid[4]. We present evidence here to show that the rate of excretion of 5-hydroxytryptamine (5HT) is similarly influenced by *p*H, being higher in acid urine (Table 1).

Data from man indicate that 5HT is normally present in the urine in low concentration[7], although larger amounts are found after parenteral administration of 5-hydroxytryptophan (5HTP)[8] and in patients with certain tumours[9]. The level probably depends to an appreciable extent on the amount of 5HTP presented to the kidney for direct renal decarboxylation. In rats used in experiments described here, the rate of 5HT excreted was greater after 5HTP injection than after 5HT (Table 1). Presumably most of the free extra-renal 5HT was either rapidly metabolized or absorbed by platelets. In these animals monoamine oxidase had been blocked with β-phenyl*iso*propylhydrazine to prevent further renal metabolism of 5HT. The absolute amounts of 5HT labelled with carbon-14 used were probably insufficient to interfere with renal haemodynamics.

It will be seen (Table 1) that there was a fairly wide variation in 5-hydroxyindole excretion between experimental groups, which may be accounted for, to some extent, by differences in such variables as depth of anæsthesia. Anæsthesia and environment of the pair of animals used in each single experiment were similar however, so that despite the between-group variation, the tendency of the 'acid rat' to excrete 5HT more rapidly than the 'alkaline rat' (Fig. 1) is probably significant.

After 5HTP administration, increased rate of 5HT excretion in the 'acid rat' is complemented by a decrease in 5-hydroxyindoleacetic acid (5HIAA) excretion and vice versa (Table 1). However, as 5HIAA is known to have an active transport mechan-

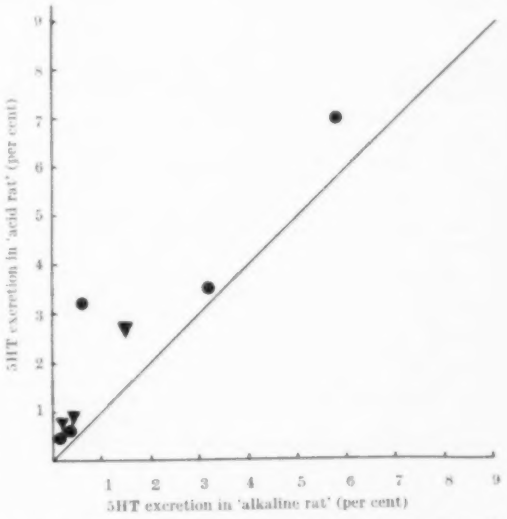

Fig. 1. Excretion of 5-hydroxytryptamine (5HT) in acid and alkaline urine expressed as percentage of total counts injected. ▲, 5HT administration; ●, 5HTP administration

ism for its renal elimination[9,10] these changes presumably reflect the absolute amounts of 5HT involved; if more is excreted by the kidney, less is available for conversion to 5HIAA. In experiments 6–8, however, in which 5HT itself was administered, the concentrations of urinary 5HT probably form too small a fraction of the total excretion of 5-hydroxyindole metabolites to produce any experimentally obvious reciprocal change in 5HIAA values. The mechanism of 5HIAA production under conditions of heavy monoamine oxidase blockade, which has been observed by many workers, is not understood.

From theoretical considerations[1], it is rather surprising that such a lipid-insoluble compound as 5HT[11] is excreted by a non-ionic diffusion mechanism. Elucidation of this problem must await further study. But one practical implication of the work that we have described is that investigations in which urinary 5HT measurements have been used as an index of 5HTP decarboxylase activity[12,13] will probably need re-evaluation.

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Influence of Sodium on the Transport of Magnesium across the Intestinal Wall of the Rat *in vitro*

Since the first description of hypomagnesaemia in adult cattle by Sjollema and Seekles[1] there have been numerous investigations into the underlying causes of this condition. Herbage analysis of the pasture where the disease has occurred shows that it is not usually due to an absolute dietary deficiency, although Norwegian workers[2] have shown that this may occasionally be so. It has been suggested that the absorption of magnesium may be impaired when cattle or sheep are suddenly moved to rapidly growing young pastures. Head and Rook[3] have suggested that this may be due to the accumulation of ammonia in the rumen, and Kemp and 'T Hart[4] have provided evidence which has incriminated high levels of potassium in the pasture at this time.

In an attempt to find out more about the factors which influence the availability of magnesium to the animal, a series of experiments has been undertaken using an *in vitro* preparation of rat small intestine[5] in which oxygenated Krebs's bicarbonate saline[6] containing 0·5 per cent glucose is circulated through the intestinal lumen, and the water and solutes which are transported to the serosal surfaces are collected below. Magnesium has been estimated, using a slight modification of the method of Mann and Yoe[7], and sodium, using an EEL flame photometer.

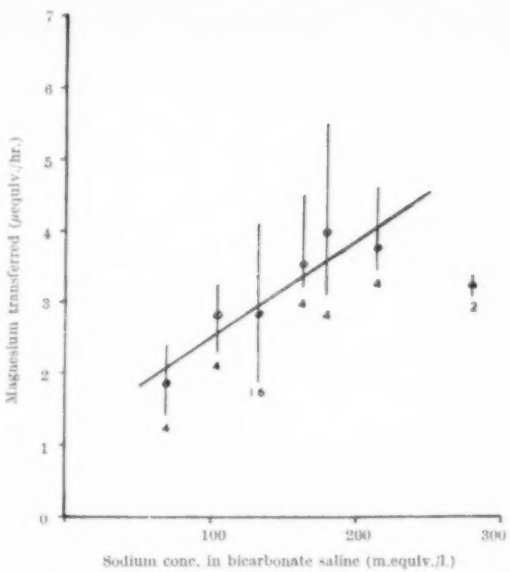

Fig. 1. Relation between magnesium transferred per hr. and sodium concentration in the bicarbonate saline. Vertical line shows range of results. Number below indicates number of experiments. Points are arithmetic means. ○, young rats; ●, old rats.

The amount of magnesium (μequiv./hr.) transported to the serosal surface was found to vary when the circulating concentration of sodium chloride was altered. This is shown graphically in Fig. 1, where the regression line for 36 readings has been drawn (magnesium transferred = 0·015 sodium concentration − 0·92; correlation coefficient $r = 0·65$; $P < 0·001$). The concentration of the other ions in the bicarbonate saline remained unaltered. The two experiments in which the concentration of sodium was highest (280 m.equiv./l., that is, an increase of 137 m.equiv./l. over Krebs's bicarbonate saline) have been omitted when the regression line was calculated. At this concentration the volume of water transported was reduced from a normal value of 2–7 ml. to less than 1 ml./hr., confirming the findings of Smyth and Taylor[5] on the effect of increasing osmotic pressure on such a preparation.

Two groups of rats were used in the experimental work, and it will be seen from Fig. 1 that the mean values for the younger group (about 12 weeks old) invariably fell above the regression line, but the means for the older group (about 20 weeks old) were below the line. This suggests that the younger group were the more efficient at transporting magnesium to the serosal surface.

The effects on magnesium transport of the addition of ammonium chloride, and increasing the potassium concentration in the circulating solution (from a normal value of 5·9 m.equiv./l.) by the addition of potassium chloride, are shown in Table 1, and are compared with the results for Krebs bicarbonate saline. It will be seen that neither of these salts

Table 1

Concentration in bicarbonate saline (m.equiv./l.)	Magnesium transported (μequiv./hr.)	No. of experiments
$K^+ - 27$	2·97	3
$K^+ - 40$	2·72	2
$K^+ - 84$	2·72	1
$NH_4^+ - 20$	3·01	2
$NH_4^+ - 100$	2·82	1
Krebs's bicarbonate saline ($K^+ - 5·9$; $NH_4^+ - 0$)	2·81	16

appears to influence the transport of magnesium under these conditions. The influence of sodium chloride on magnesium transport is therefore probably due to the sodium rather than to the chloride ion, since the chloride was common to all three salts.

It is interesting to note that the association between sodium and magnesium transport across the intestinal wall, reported here, is similar to that recently described for the human kidney[6], where the rate of excretion of magnesium was found to vary directly with the concurrent excretion of sodium chloride.

The relation of these findings to ruminant hypomagnesæmia is difficult to evaluate, since the conditions in this *in vitro* preparation of rat small intestine are very different from those of the ruminant gastrointestinal tract, although it does suggest that attention should be given to the influence of varying sodium-intake on magnesium absorption in the intact animal.

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Clinical Application of a Serological Method for the Determination of Human Chorionic Gonadotrophin

It was early observed that prolonged administration to animals of gonadotrophic hormone from human pregnancy urine was accompanied by gradually diminished effects[1]. This phenomenon has been found to be due to the formation of an antigonadotrophic factor demonstrable only by its capacity to impair the gonadotrophic reaction in rodents[2]. Previous to our earlier report[3], there had been no demonstration of the antigonadotrophic factor by serological *in vitro* methods. Precipitating and complement-fixing antibodies had been obtained by immunization of rabbits with gonadotrophic hormone prepared from human pregnancy urine[4,5]. These antibodies, however, were shown to be due to contaminating, antigenically active substances[6].

In contrast to these investigators, we have been able to demonstrate that human chorionic gonadotrophin can stimulate the production, demonstrable *in vitro*[3], of antibodies against itself. This was accomplished by the inoculation of a purified human chorionic gonadotrophin preparation (Gonadex-Leo, supplied by courtesy of Dr. Högberg, AB Leo, Hälsingborg, Sweden) together with an adjuvant into a heterologous species (rabbit). The presence of human chorionic gonadotrophin antibodies in the rabbit sera was demonstrated with the complement fixation test. With these antisera, human chorionic gonadotrophin could then be determined in serum as well as in the urine of pregnant women by means of this serological test. Two other reports, in principle confirming our results, have since been published. These showed that the estimation of human chorionic gonadotrophin in urine was possible with the precipitin test[7] and the hæmagglutination inhibition reaction[8].

In further experiments we have been particularly interested in evaluating the sensitivity and specificity of our serological procedure for the determination of human chorionic gonadotrophin with a view to its clinical applicability. From practical as well as physiological considerations, we have preferred to analyse serum rather than urine.

Preparation of antisera. Twelve rabbits were immunized, each with 12,500 I.U. of human chorionic gonadotrophin in adjuvant (10 parts of the hormone in saline, 8·5 parts paraffin oil and 1·5 parts 'Arlacel A', the mixture containing 10 mgm. of finely powdered *Mycobacterium butyricum* per 100 ml.) administered in a total volume of 20 ml. on three occasions at intervals of three weeks. The mixture was given at four sites subcutaneously and intramuscularly. A booster injection of 3,000 I.U. of the hormone in saline was given intravenously four to six weeks after the last inoculation. Blood was withdrawn by cardiac puncture one week after the booster injection. Serum was separated, heated at 56° C. for 30 min. and stored at −20° C.

Serological technique and standardization of antisera. The rabbit sera were tested for the presence of human chorionic gonadotrophin antibodies in complement fixation tests against the hormone dissolved in sera from non-pregnant individuals. The tests were carried out as 'chess-board' titrations according to the plate technique of Fulton and Dumbell[9] as modified by Svedmyr, Enders and Holloway[10]. Twofold serial dilutions were employed with barbiturate buffer as diluent. Simultaneous complement titrations with antigens, antisera and diluent were included in each experiment to rule out false positive reactions due to anticomplementary effects.

All antisera were tested against sera from non-pregnant women. Most rabbit sera gave negative results. With a few antisera positive reactions in low-antiserum titres of the type described earlier were encountered[3]. These reactions could be completely overcome by means of a simple absorption procedure[3].

The antisera were then tested with a solution containing 1,500 I.U. of the hormone; its concentration was checked against the international standard. A typical 'chess-board' titration is shown in Table 1. The hormone solution diluted 1/6,400 still gives positive reactions, which implies that with this anti-

Table 1. 'Chess-board' Titration of Human Chorionic Gonadotrophin with Serum from Rabbit immunized with the Hormone

Antigen	Dilution of antigen	Dilution of antiserum 8	16	32	64	128	256	512
Human chorionic gonadotrophin 1,500 I.U. per ml.	50	+	+	+	+	−	−	−
	100	+	+	+	+	+	−	−
	200	+	+	+	+	+	+	−
	400	+	+	+	+	+	+	−
	800	+	+	+	+	+	+	−
	1,600	+	+	+	+	+	+	−
	3,200	−	+	+	+	+	+	−
	6,400	−	−	+	+	−	−	−
	12,800	−	−	−	−	−	−	−

serum 0·25 I.U. of human chorionic gonadotrophin per ml. can be determined. The maximal titres of the hormone solution varied from 3,200 to 12,800. From Table 1 it is apparent that antiserum diluted 1/32 is suitable for carrying out quantitative determinations of the hormone in a routine procedure. This has also been confirmed in 'chess-board' titrations with specimens from pregnant women.

Clinical investigations. Blood samples were collected from 194 patients. Serum was separated, heated at 56° C. for 30 min. and stored at −20° C. until examined. 148 women were pregnant. Pregnancy was diagnosed by gynæcological examination and in early cases by biological pregnancy tests[11]. (The biological pregnancy tests were performed at the Hormone Laboratory of the Department of Obstetrics and Gynæcology, Karolinska Sjukhuset.) As all samples were collected 3–7 months before testing, all cases were also checked by follow-up. With the serological determination procedure of chorionic gonadotrophin, all specimens from pregnant women gave positive results. No false positive reactions were found. Fig. 1 illustrates the quantitative results obtained with sera from pregnant women varying in gestational stage from 5 to 42 weeks. The titres vary from 2 to 1,024 corresponding to 0·7 to 340 I.U. of hormone per ml. serum. The highest titres were observed during the first trimester. High values were, however, also found late in pregnancy.

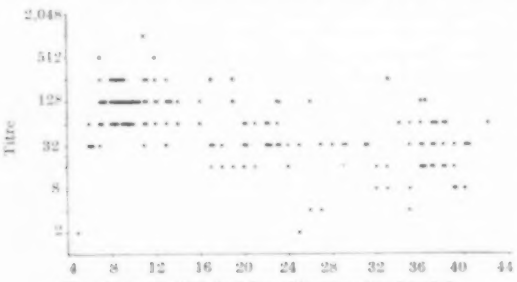

Fig. 1. Results of serological determination of human chorionic gonadotrophin in serum of 148 pregnant women. (According to standardization tests, a minimal amount of 0·35 I.U. of the hormone per ml. could be determined with the antiserum used)

These results indicate that the serological procedure presented here is a sensitive and specific method for the determination of human chorionic gonadotrophin. Its suitability for the diagnosis of pregnancy seems apparent. The fact that the test can be performed on serum increases the clinical importance of the quantitative data obtained. Work is now in progress on quantitative serological analyses of human chorionic gonadotrophin in serum in various pathological conditions. We are also planning simultaneous quantitative biological and serological determinations of the hormone.

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Subjective Analysis of Saccadic Eye Movements

In the course of an investigation into the mechanics of eye movements, using mainly electrical recording methods[1], some of the findings have been checked by a simple subjective method. This enables an observer to examine his own saccades, which he sees traced out before him in the form of displacement-time curves.

The subject views, from a distance of about 50 cm., a cathode ray oscilloscope, on which is a straight horizontal line, generated by a time-base running at a velocity between 20 and 50 cm./sec. When small downward vertical saccades of a few degrees extent are made, a tracing of the type shown on the left of Fig. 1 is seen, and when upward vertical movements are made, the tracing is usually that shown on the right. An explanation of how the effects are produced follows that given by Crookes[2], to explain the visual sensations accompanying saccadic movements across a television screen.

The effects are best seen in a darkened room, and are particularly clear for downward movements which start a few centimetres above the line, and end on the line, in which case the overshoot is seen just above the level of the line. If much larger saccades, of about 30°, are made, starting above the oscilloscope and ending on the line, the overshoot is seen to be only slightly larger than for 3° saccades (average values $\frac{1}{2}$° and $\frac{1}{4}$° respectively). With a double-beam instru-

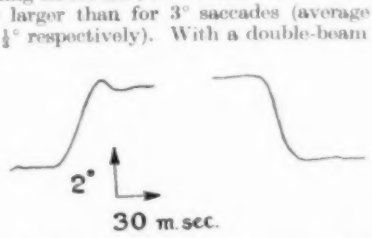

Fig. 1. Vertical saccades recorded with capacitance gauge

ment, two parallel curves appear to be traced out by the two spots.

When observation is made by reflexion in a mirror, so that the oscilloscope spot appears to travel from right to left, the traces are now reversed. Horizontal eye movements can be examined by either tilting the head, leaving the instrument fixed, or by rotating the oscilloscope so that the line is vertical.

Twelve subjects have perceived the effects, without difficulty, and have been able to estimate the duration of their own saccades and the dependence on the amplitude of the saccade. Reports differ slightly in the amount of overshoot, but agree that it is larger in downward movements, and that its magnitude is largely independent of the extent of the movement. In horizontal saccades this asymmetry appears to be less pronounced.

These subjective observations, in which there is no interference with the eye in any way, are consistent with my own experimental results, and with those of Byford[3], who has recorded eye movements by attaching a lamp to a contact lens. They do not support the model of saccadic eye movements put forward by Westheimer[4], on the basis of his own measurements.

A detailed analysis of the overshoot phenomenon is to be reported elsewhere.

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Breakdown of Seminal Glycerylphosphorylcholine by Secretions of the Female Reproductive Tract

In the course of experiments on the metabolism of glycerol by ram spermatozoa, the seminal plasma was found to contain high concentrations of a substance estimating as glycerol[1]. This was identified as a glycerol complex, namely, glycerylphosphorylcholine, which was shown to occur in ram seminal plasma in a concentration of more than 1 per cent, and in the semen of the bull, goat, stallion, man and rabbit in lesser amounts[2]. Despite its high concentration in the seminal plasma, however, ram spermatozoa are unable to metabolize glycerylphosphorylcholine[2], and its physiological significance has hitherto been unknown.

On the other hand, it is well established that ram spermatozoa can utilize free glycerol, or phosphoglycerol, under aerobic conditions with the formation of lactic acid, which can be further oxidized to carbon dioxide and water[1,2]. It occurred to us, therefore, that there might be an enzyme in the secretions of the female tract capable of splitting choline from the glycerylphosphorylcholine molecule and thus liberating glycerol or phosphoglycerol that could be utilized by the spermatozoa, since conditions in the female tract are believed to be essentially aerobic[4]. This has proved to be so and the evidence is outlined in this preliminary communication.

Secretions were expressed from the uterus and Fallopian tubes of freshly slaughtered ewes, or washed out with Ringer solution. When 0·5 ml. of this fluid was incubated at 37° C., either overnight (7 experiments) or for 3 hr. (14 experiments), with 0·1–0·5 ml. of ram seminal plasma, a highly significant ($t = 5·2$, d.f. = 12, $P < 0·001$; and $t = 4·5$, d.f. = 26, $P < 0·001$ respectively), though somewhat variable, increase in free choline, as estimated by methods previously described[2], occurred. On the average, about 30 per cent of the glycerylphosphorylcholine was broken down in 3 hr. and about 50 per cent overnight. Thus appreciable quantities of metabolizable end-products (namely, glycerol or phosphoglycerol) are likely to be produced following the introduction of seminal glycerylphosphorylcholine into the female tract. The variability in free choline liberated is not unexpected, since it was only possible in these preliminary tests to calculate the results in terms of the volume of fluid washed from the female tract rather than on the basis of dry weight or protein content. Large variation in the composition of the uterine fluid itself might also be expected, depending on the stage of oestrous cycle[5].

No significant increase in free choline was found when the secretions of the reproductive tract of the ewe, or the seminal plasma of the ram, were incubated separately. The increase in free choline on mixing the secretions followed a fairly linear course during 3 hr., and could be almost exactly accounted for by the disappearance of glycerylphosphorylcholine. Thus, in three experiments a mean of 426 μgm. of free choline was liberated per ml. of incubation medium and 392 μgm. of glycerylphosphorylcholine–choline lost.

The liberation of free choline is clearly not due to bacteria, since it was unaffected by bacteriostatic concentrations of a mixture of penicillin and streptomycin. On the other hand, the increase in free choline was completely abolished by heating the secretions of the female tract for 5 min. at 100° C., suggesting that an enzyme, probably a diesterase similar to that found in the liver[6], is responsible. Similar investigations have shown that the enzyme is also present in the secretions of the reproductive tract of the cow and the sow.

In view of the apparent widespread occurrence of this enzyme in the female secretions, it is suggested that glycerylphosphorylcholine might be an important source of energy for spermatozoa in the female tract after copulation, despite the fact that spermatozoa themselves may not be capable of breaking down the intact molecule. It is interesting in this regard to compare glycerylphosphorylcholine with the better-known seminal constituent, fructose[7]. This sugar, which is readily utilized by spermatozoa, is produced by the seminal vesicles or prostate and is not normally mixed with the spermatozoa until after ejaculation[7]. Glycerylphosphorylcholine, on the other hand, is chiefly found in the epididymal fluid of the larger species[2], and, although always in intimate contact with the spermatozoa, can only be utilized by them after the semen has come into contact with the female secretions. The occurrence of a glycerylphosphorylcholine-splitting enzyme in the female secretions would seem to constitute a rather novel method of ensuring that spermatozoa have an additional source of energy available to them in the female tract.

The enzyme is now being further characterized, and full details of the work will be published elsewhere.

We are indebted to Prof. C. W. Emmens for his interest in this work, and to Mr. P. Bryden of

the New South Wales State abattoirs for his co-operation in obtaining experimental material. The work has been supported by grants from the Planned Parenthood Federation of America and the Wool Research Fund.

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Lipoprotein Composition of the Film lining the Lung

Small bubbles ($\sim 50\mu$ diam.) in air-saturated water usually contract and disappear within a few minutes. In similar circumstances, however, small bubbles derived from animal lungs are stable. This is due[1] to their surface tension being reduced to 0·05 dyne/cm. or less by an insoluble surface film. This film is derived from the original film lining the lung alveoli; its (oven-dry) mass is about $6{\cdot}4 \times 10^{-7}$ gm./cm.^{2}. *In situ* it annuls the tension of the sharply curved alveolar surface, which would otherwise give rise to transudation from the blood or to atelectasis[2]. For various reasons the film was at first thought to consist of mucoprotein.

Specimens of the substance lining the bubbles have now been isolated. Water was forced down the main bronchus into the excised lung of a cow, and was then allowed to well out, laden with bubbles. These bubbles were then washed with ten changes of water, so as to remove all dissolved matter and suspended solids. A sample of the washed froth, dried at 40° C., left a pale brown solid of waxy consistency.

This residue was examined in the form of a cast film on a potassium bromide plate by infra-red absorption spectroscopy, a model 137 Perkin–Elmer spectrophotometer being used. The spectrum, and that of a mixture of purified egg lecithin (95 per cent) and gelatin (5 per cent) for comparison, are shown in Fig. 1. Qualitatively, the curves are identical. The relative intensities of the ester carbonyl bands at

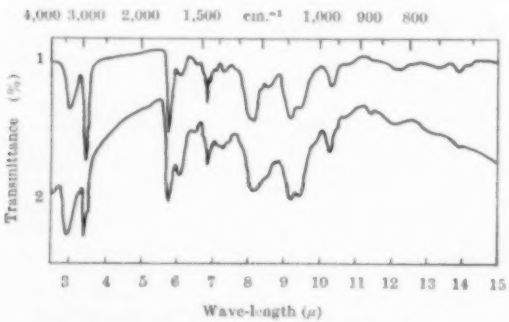

Fig. 1. Percentage transmission (on arbitrary scale) of infra-red radiation through (curve 1) lung bubble lining substance and (curve 2) mixture of 95 per cent lecithin and 5 per cent gelatin

5·75μ and the amide bands at 6·1μ and 6·5μ in the two spectra suggest that the proportion of protein in the bubble lining is about 1 per cent. The presence of small amounts (< 1 per cent) of other lipids or of carbohydrates cannot be excluded, but it is clear that the lining film consists in the main of a lecithin–protein complex; the very low value of the protein content suggests that some of the lecithin present may be adventitious.

Small stable bubbles have also been obtained from other sources. They are formed, for example, when dry powders of a bacterial lipopolysaccharide[3], of thromboplastic lipoprotein[4], or of acetone-washed egg yolk, are wetted. They may also be obtained by wetting acetone-dried or freeze-dried tissues (muscle, brain, etc.).

Lipoprotein complexes are known to form readily[5,6]. When, for example, lecithin (4 gm.) and gelatin (1 gm.) are ground to a paste with water, and the paste is dried with acetone, a leathery porous substance results; this, when wetted and squeezed under water, yields stable bubbles. It may therefore be that some of the bubble-stabilizing substances found in dried tissues are artefacts which are not present *in vivo*.

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Effect of Exposure to Sun and Exercise on Heat Tolerance Coefficient in Murrah Buffalo Calves

In continuation of our previous work[1], this experiment was designed to find out the effect of exposure to sun and exercise on heat tolerance coefficient. Eight Murrah buffalo calves, varying between 8 and 12 months of age, constituted the experimental material. These calves were randomly divided into two groups of four each. One group was exposed to sun, while the other ran at a speed of four miles per hour as recorded by the distance covered in a given time. The calves in each group acted as their own control. These experiments were conducted at 12 noon for half an hour on six consecutive hottest days in the month of May. The atmospheric temperature during test hours ranged between 92 and 105° F. and relative humidity between 28 and 47 per cent. The conditions of management of these calves has been given in detail[2].

The heat-tolerance coefficient was calculated daily for each animal, as control and after exposing them to sun or exercise, by Rhoad's formula[3]. The variations were analysed statistically[4].

Table 1 indicates mean value, variance, standard deviation, and coefficient of variation of the atmospheric temperature, relative humidity and heat-tolerance coefficient. There seems to be a degree of consistency in the mean values of the controls of the

Table 1. Heat Tolerance Coefficient

	Temperature		Humidity		First group		Second group	
	Under shade	In sun	Under shade	In sun	Control (in shade)	Exposed to sun	Control (in shade)	Put to exercise
Mean	93·66	98·00	42·00	32·66	92·33	80·80	94·04	65·00
Variance	1·48	16·40	10·40	43·48	62·14	68·86	19·52	185·73
Standard deviation	1·21	4·04	3·22	6·52	7·88	9·31	4·42	13·62
Coefficient of variance (per cent)	1·29	4·12	7·66	20·11	8·53	11·5	4·90	20·95

two groups, but F value indicates ($F_{24,24} = 3{\cdot}1$; $P_{1\%} = 2{\cdot}66$) that the variation between the controls of the two groups is significant. As such these values could not be pooled together to test the differences between the two different groups. However, the variance ratio in the first and the second group when compared with their own controls were 1·39 and 9·51 respectively ($F_{23,23}$ 5 per cent = 1·98). Since variance of heat tolerance coefficient in the first group was not significant, the t test was applied for testing the differences between the two means ($t_{24} = 2{\cdot}39$; P_{24} 5 per cent = 2·06). These two mean values were found to be significant.

Table 2 indicates that there were significant differences in heat tolerance coefficient of the calves before and after exposure to the sun. The calves of the other group when put to exercise showed significant differences in their heat tolerance between themselves, between days and between treatment. Every animal behaved differently for its capacity to withstand the thermal stress on different days to the exercise given.

Table 2. Analysis of Variance

Sources of variation	d.f.	Mean square	
		First group Effect of exposure to sun	Second group Effect of exercise
Between animals	3	158·58	61·40*
Between days	5	187·08	375·38*
Between treatment	1	1,598·52*	10,120·84*
Between animal × days	15	43·62	29·21*
Between animal × treatment	3	47·63	31·83*
Between days × treatment	5	13·62	403·45*
Between animal × days × treatment	15	76·65	7·23

* Significant at 1 per cent level.

The buffalo calves after exercise were observed seeking the shade and in distress characterized by licking, panting and general restlessness. Drooling appeared when the increased respiratory activity proved unsuccessful in stabilizing body temperature. These are physical homœothermic mechanisms which ease the burden of heat load on the animal[5]. The ability of the buffalo calves to withstand the tropical heat, especially when exposed to the sun or put to exercise, seemed to decrease, perhaps because of the increased heat production and absorption[6]. The black pigmented hide absorbs the infra-red rays of solar radiation and thus limits the animal's adaptability to exposure to sunlight. In the shade, however, the black coloration aids heat dissipation[7]. Adaptation to hot humid climate is characteristic of the buffaloes. The thick skin of the buffalo calves may prevent heating of the body from hot air and by radiation from the sun or hot ground. The buffalo calves, although surviving in hot zones when humidity is high, essentially require shade and cooling systems for their comfort[8].

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HÆMATOLOGY

A Notation for the Gm Groups

The following met in Rouen in April 1960 to discuss notation and other matters regarding the Gm serum protein groups of man: A. Eyquem, Institut Pasteur, Paris; H. Fudenberg, Rockefeller Institute, New York; R. Grubb, Bacteriological Institute, Lund; M. Harboe, Institute for Thrombosis Research, Oslo; S. Lawler, Galton Laboratory, London; J. Moullec, Centre National de Transfusion Sanguine, Paris, represented by C. Henry; L. Podliachouk, Institute Pasteur, Paris; C. Ropartz, Centre Départemental de Transfusion Sanguine, Rouen; A. Steinberg, Western Reserve University, Cleveland; A. Tiilikainen, Department of Serology and Bacteriology, University of Helsinki. The following statement has been prepared.

It is increasingly apparent that the Gm system is complex and our aim is to minimize confusion originating in differing nomenclature or standards.

To be accepted as part of the Gm system a character must be shown to be contained in the gamma-globulin fraction, and its relationship to the known Gm factors demonstrated by genetical and/or population studies.

The characters to be considered at the present state of knowledge are Gm(a), Gm(b), Gm(x) and Gm-like as originally described in references 1–6 respectively.

Symbols for genotypes and phenotypes should be clearly distinguishable. In conformity with the suggestions of Ford[7], we will adhere for Gm notation to the two following rules: (1) the use of italics for gene symbols and the use of ordinary type for phenotypes; (2) the use of suffixes for genes, but not for phenotypes. Example: Gm^a for the gene, Gm(a +) for the phenotype.

The use of gene symbols containing the suffixes a_1 and a_2 for specified characters has been suggested[8]. This proposal is now withdrawn. At the present state of knowledge no further suggestions for the gene symbols seem warranted.

The notation which will be used for the phenotypes now known is as follows: Gm(a + b + x +), Gm(a + b + x −), Gm(a + b − x +), Gm(a + b − x −), Gm(a − b + x +) (Henningsen, unpublished observations confirmed by Harboe), Gm(a − b + x −), Gm(a − b − x −). The type Gm(a − b − x +) has not yet been encountered. This notation can readily be expanded to adopt new phenotypes as they may be found and/or be included in the Gm system. To denote the Gm-like character, Gm-like (+) or Gm-like (−) is added; for example, Gm(a + b + x −) Gm-like (+). The term Gm-like is regarded as temporary. So-called intermediates may be signified by ± ; for example, Gm(a ±). The gamma-globulin-levels in sera of unusual phenotypes should be determined and given.

The terms anti-Gm(a), anti-Gm(b) and anti-Gm(x), to which the classical noncommittal term 'reagin' may be added, will be used to denote the specificities of the substances (usually, if not always, macroglobulins) causing the agglutination of red cells coated with human incomplete antibodies.

Samples of normal human sera of at least some of the known Gm-types, which can be used as standards, will be supplied on request by me. Standard Gm-like (+) and Gm-like (−) samples are obtainable from A. Steinberg, Department of Human Genetics, Western Reserve University, Clevoland 6, Ohio, U.S.

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Formation of Hæmosiderin and its Relation to Ferritin

Support for the hypothesis that the protein moiety of hæmosiderin is the same as that of ferritin can be found in the literature[1,2]. Iron tetrad (or, more recently, 'hexad'[3,4]) structures in a protein matrix characteristic of ferritin have been reported in electron photomicrographs of tissue sections variously interpreted as ferritin, hæmosiderin, aggregates of ferritin, etc.[3,5,6]. It is not uncommon, therefore, to consider both ferritin and hæmosiderin as being more or less identical. However, the results of our biochemical and histochemical work lead to opposite conclusions[7,8].

Before commenting further, it should be emphasized that in biochemical terms, as originally defined by Laufberger[9], the fundamental property that distinguishes ferritin from hæmosiderin is the solubility of ferritin in water. It must also be recognized, despite the common misconception to the contrary, that ferritin does take the Prussian blue stain[10]. Failure to recognize and to apply these principles introduces the possibility that 'hæmosiderin' in tissue sections might consist partially or entirely of ferritin.

We have observed with biochemical and histochemical techniques that, as the water-extractable ion (ferritin) of rabbit liver approaches 200 mgm. per 100 gm. of tissue, Prussian blue-positive granules (hæmosiderin) form in the parenchymal cells. This phenomenon is clearly observed when the iron is administered as iron dextran; with saccharated iron oxide, the phenomenon is also reproducible relative to the parenchymal cells. In the Kuppfer cells, there is in addition, with the latter preparation an accumulation of stainable insoluble iron at an early stage. This Kuppfer cell iron differs in several respects from that of the parenchymal cells; it is not under consideration at present.

At levels of iron load just preceding that at which the typical Prussian blue-positive hæmosiderin granules appear, the formation of several intracytoplasmic vacuoles in the parenchymatous cells adjacent to the portal regions can be observed. These vacuoles are 1–2μ in diameter, have irregular borders, tend to be in proximity to the nuclei and, most important, give a faint blue homogeneous colour on staining for iron. As the iron load is increased, the larger of these vacuoles begin to show typical dense, dark-staining Prussian blue granules. At this point, one can still identify faint light blue-staining material at the periphery of these vacuoles. With increasing iron load, only typical Prussian blue-positive hæmosiderin granules are evident. The light blue material observed at earlier stages can be removed by water extraction of cubes of liver (1–2 mm.^{3}). The quantity of iron recovered in the extract corresponds closely to the ferritin content of the liver, as determined by biochemical methods. The dense, dark blue-staining granules remain unaltered. We have recorded these events by colour photomicrography; this work will be published elsewhere.

From the above, the lack of clear-cut distinction between hæmosiderin and ferritin by electron and/or light microscopy on tissues which have not had the ferritin removed by water extraction can be explained. For example, a recent electron photomicrograph by Bessis and Breton-Gorius[11] shows sections composed of electron-dense particles in a matrix, linearly arranged in a crystal lattice. This, as well as publications by Richter[12] and Kerr and Muir[3], also show aggregates of electron-dense iron particles with little or no matrix. They are variously interpreted as being ferritin crystals, different forms of hæmosiderin, aggregated ferritin, etc. As our work on granules isolated after extraction of ferritin indicated that the two compounds were chemically distinct, we submitted our preparations to Dr. G. W. Richter for electron microscopy. The electronmicrographs showed closely aggregated electron-dense particles, but neither ferritin crystals nor even isolated 'tetrads' were evident. This collaborative work is being extended and will be published separately.

These observations indicate that hæmosiderin and ferritin are not only chemically but are also structurally dissimilar. They also suggest strongly that the hæmosiderin granule, at least of the rabbit liver parenchymal cell: (1) is a relatively amorphous condensation of electron-dense iron particles into an essentially protein-free aggregate; (2) that it consists mainly of ferric hydroxide; (3) that it originates in liver cell vacuoles through a process of degradation of the protein matrix of ferritin; (4) that the linearly arranged iron particles in a matrix correspond to the faint blue-staining material we have observed histochemically in parenchymal cell vacuoles. Because of the water-solubility of the latter material, we conclude it represents ferritin. This concept leaves room for intermediate stages between native ferritin

and the apoferritin-free aggregates of ferric hydroxide particles.

Therefore it is recommended, in order to bring anatomical and biochemical nomenclature into agreement, that the term 'hæmosiderin' should be applied only when the compound under investigation is known to be water-insoluble. This division may be arbitrary in an anatomical sense, but it is easily and accurately applied and will preclude the misconception that hæmosiderin and ferritin are identical.

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An Attempt to produce Hæmolytic Disease in Lambs

RENDEL[1] attempted to produce hæmolytic disease of the new-born lamb by injecting 8 pregnant ewes with blood taken from the rams to which they were mated. As a result, 4 of the ewes produced immune antibodies which reacted with the red cells of their mates; but their lambs did not develop hæmolytic disease even though at least 2 of them ingested colostrum-containing antibodies which reacted weakly *in vitro* with their respective red cells. In these cases, no antibody could be detected on the lambs' red cells, and Rendel concluded that if hæmolytic disease occurred in lambs it must be rare.

This communication describes an experiment carried out on similar lines to those of Rendel. A ewe was chosen which one year previously had been immunized with the blood of a certain ram and which had made a strong immune antibody to the ram's red cells. This ewe was mated to the ram, and during the later stages of pregnancy was given a booster injection of the ram's blood which resulted in a sharp rise in serum antibody titre from only a trace reaction to a titre of 1/16,000. Twin female lambs were born to the ewe after the normal pregnancy time, and blood samples were taken from them before they had sucked, and at 4, 7, 10 and 24 hr. after sucking and at intervals thereafter. In addition, blood serum and milk samples were taken from the ewe before and after parturition.

Both the serum and colostrum samples taken from the ewe at the time of parturition were titrated against the lambs' precolostrum red cells, using a simple hæmolytic test. To 1 drop of a 2 per cent red cell suspension in saline, 1 drop of the serum or colostrum at the appropriate dilution was added. These were mixed and left for 15 min. when 1 drop of undiluted rabbit complement (rabbit serum, absorbed with sheep red cells) was added. The test was left at 32° C., shaken at hourly intervals and read after 4 hr. The highest dilution of antiserum showing definite hæmolysis was taken as a measure of the strength of the antibody. Using this test, it was found that the dam's serum and colostrum reacted with the red cells of both lambs to a titre of about 1/8,192–1/16,384. The samples of red cells taken from the lambs were therefore tested to see whether they were 'sensitized'. They were washed once in saline and to 1 drop of a 2 per cent saline suspension of the red cells, 2 drops of rabbit complement diluted ½ were added and the test incubated at 32° C. Readings were taken after 1 hr. No hæmolysis was observed in the precolostrum or 4-hr. red cell samples; but the red cells taken from the lambs 7 and 10 hr. after sucking showed partial hæmolysis. The 24-hr. samples showed complete hæmolysis as did samples taken 5 days after birth. Nine days after birth the lambs' red cells again showed partial hæmolysis on the addition of complement and by the seventeenth day there was no evidence of sensitization. The hæmatocrit of the blood samples fell sharply during the first 5 days after birth (from 44 to 27 per cent in one lamb and from 47 to 25 per cent in the other lamb); but a similar drop was observed in blood samples taken from control lambs during the first week after birth, so this was considered to be of no significance. An osmotic fragility[2] test was made on the red cells of one of the lambs taken 5 days after birth, that is, at a time when the cells were well coated with antibody, but there was no evidence that their fragility was in any way different

Table 1. ANTIBODY TITRES AGAINST LAMBS' RED CELLS

Time of sample	Lamb No. *M*292			Lamb No. *M*293		
	Serum titre* of dam	Colostrum titre* of dam	Serum titre* of lamb No. *M*292	Serum titre* of dam	Colostrum titre* of dam	Serum titre* of lamb No. *M*293
Pre-sucking	8,192	16,384	0	16,384	16,384	0
4 hr. post-sucking	—	—	0	—	—	2
7 hr. ,,	—	8,192	0	—	8,192	16
10 hr. ,,	—	—	64	—	—	64
24 hr. ,,	—	1,024	64	—	1,024	64
2 days ,,	8,192	256	32	8,192	128	64
5 days ,,	—	—	8	—	—	8
9 days ,,	2,048	—	0	2,048	—	0
17 days ,,	—	—	0	—	—	0
23 days ,,	1,024	—	0	1,024	—	0

— Not tested. * Titre expressed as the reciprocal of the highest dilution of antiserum giving definite hæmolysis.

from that of the red cells of the control lambs of comparable age. Both lambs in fact showed no abnormal symptoms and grew and developed normally.

When the lambs were about 2 months old, their red cells were tested against titrations of their own sera, and against their dam's serum, and colostrum samples taken during the first days after birth. Table 1 shows the results. Antibody appeared in both lambs' sera at about the same time that their red cells began to show sensitization, reached maximum levels at 10 hr. and then declined in titre until by the ninth day none was detectable.

0·4 ml. of red cells from one of the 2-month-old lambs was labelled with chromium-51 (ref. 3), incubated for 20 min. at 37° C. in 8 ml. of a 1-in-4 dilution of the dam's serum taken at parturition, washed and injected back into the same lamb. A blood sample taken 5 min. after the injection showed only a trace of radioactivity, indicating that the injected red cells had all been quickly eliminated from the circulation. This experiment was repeated, only this time the lamb's red cells were incubated in a 1-in-4 dilution of its own serum taken 1 day after birth when it had an antibody titre of 1/64. The red cells were again quickly eliminated from the circulation.

The situation was therefore found where two lambs failed to show any symptoms of haemolytic disease even though their red cells were strongly sensitized by antibodies ingested from the dam via the colostrum. A similar condition was reported in calves by Chavez[4], who fed a calf with colostrum to which had been added anti-ox antibody produced in rabbits, and demonstrated that its red cells became coated with antibody. The calf showed no symptoms of haemolytic disease. Kiddy, Stone, Tyler and Casida[5] isoimmunized cows with a bull's blood; but although the dams' sera and colostra reacted with the calves' red cells in their experiments, no antibody to the calves' own red cells could be found in the calves' sera and no antibody could be detected on their red cells. From these findings they suggested that the mechanism protecting the new-born calf was the absorption or neutralization of ingested antibodies by tissue or soluble antigens, thus preventing the antibodies from reaching the calf's erythrocytes and causing their destruction. This could not be the explanation of the failure to produce haemolytic disease in the lambs, for not only were the red cells coated with antibody, but at the time at which there was maximum *in vivo* sensitization there was also free antibody circulating in the plasma. The fact that the lamb's red cells when sensitized with this free antibody were rapidly eliminated from the circulation of the lamb when it was 2 months old would suggest that the protective mechanism might lie in the mode of action of the reticulo-endothelial system of the newly born lamb or a deficiency in some serum factor which causes destruction of sensitized cells.

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RADIOBIOLOGY

Strontium-90 in Human Teeth

The ultimate concern in strontium-90 fall-out monitoring is the amount of the nuclide assimilated in man. Several world-wide studies have been made to determine the concentration of this fission product in human bone. Kulp[1] defined the strontium-90 content of bones of children and adults up to 1959, while Bryant published similar United Kingdom bone results for 1958[2,3] and early 1959[4].

Since bone is usually obtained at autopsy, sample collection is limited and complicated for local studies. Strontium-90 analysis of human teeth, especially deciduous teeth, is simpler from the point of view of collection and preparation.

Kalchar[5] first suggested a world-wide deciduous tooth radiation census. He stated that strontium-90 assays of teeth would reflect the fall-out level at or near the time of birth. There is some evidence that teeth may also reflect, to a lesser degree, fall-out levels up to the time of removal. Armstrong[6] and other investigators found calcium-45 and phosphorus-32 in mature animal teeth shortly after administration of the radionuclides. The relative amounts of uptake of these radionuclides were: bone > dentine > enamel.

The growth chronology of deciduous and permanent teeth was reported by Wheeler[7]. Each type of tooth has a different chronology, and there are also variations between individuals. Deciduous teeth begin to form before birth, but enamel and roots are not completed for many months. Permanent teeth are not completely calcified for several years after eruption.

Only a few teeth analyses have been reported, due to insensitive methods of analysis and relatively small amounts of strontium-90 in teeth formed in the early 1950's. The highest result of three analyses reported by Hardy[8] was 0·79 ± 0·12 μμc. strontium-90/gm. calcium.

Bryant[9] recently reported the strontium-90 content of sound 9- to 13-year permanent premolars and 16- to 21-year third molars. The strontium-90 concentration for both groups lay in the range 0·1–0·4 μμc./gm. Although there was a rough inverse correlation with age, he reported that the material was too limited to be biologically significant.

The method used by Bryant is typical of most strontium-90 procedures used to date. After addition of strontium carrier, the strontium-90 and natural calcium from 40-gm. batches of teeth were precipitated as oxalates and then as carbonates. Strontium was separated from calcium by repeated precipitations as nitrate. Strontium carbonate was finally precipitated and mounted for counting.

Teeth results reported here were obtained by an improved method of analysis. One hundred and twenty-one teeth were collected in late 1959 and combined to 81 samples before analysis. After a minimum of analytical steps, the final strontium-90 content was determined by counting carrier-free yttrium-90. The method was thoroughly investigated and reported in a previous general fall-out survey[10]. Preparation of teeth included an initial 3-min. soaking in 1 : 10 hydrochloric acid to remove surface film, followed by rinsing with distilled water. Fillings were removed and teeth were air-dried overnight before weighing.

Initial experiments proved that direct dissolution of teeth and co-precipitation of calcium and strontium as oxalates were preferable to ashing. Teeth were dissolved in 50 ml. of 1 : 1 hydrochloric acid. After complete solution, the sample volume was increased to 600 ml. by addition of distilled water. Three grams of oxalic acid were added, and the solution was heated to 80–90° C. Oxalates were precipitated by gradual addition of 1 : 1 ammonium hydroxide, while stirring, to *p*H 5–6. After overnight digestion, the precipitate was separated by vacuum filtration through Whatman No. 42 filter paper. The oxalates were fired to oxides in a muffle furnace at 650° C. The final solid was then dissolved in 50 ml. of 0·08 *N* hydrochloric acid, prior to strontium-90 analysis.

Strontium-90 analysis was obtained by counting the carrier-free yttrium-90 daughter, after an extraction procedure. The 50-ml. sample was first stripped of yttrium-90 by two extractions with equal volumes of 20 per cent di-2-ethylhexyl phosphoric acid in toluene. The yttrium-90 daughter of strontium-90 was allowed to build up to the equilibrium-level over a period of two weeks and was then extracted from the original sample with 5 per cent di-2-ethylhexyl phosphoric acid. Yttrium-90 was removed from the organic layer by extraction with 3 *N* nitric acid. The acid was then evaporated and plancheted. All samples were counted two or more times in a low-background counter to verify the yttrium-90 decay.

Results of this preliminary analysis are shown in Table 1. Due to the small number of samples in each age-group, the types of teeth were not reported. The large errors shown in the last column are due to analyses of individual teeth weighing as little as 0·1 gm. This experience indicates that further sample composites should weigh not less than 2 gm.

Table 1. STRONTIUM-90 ANALYSES OF 121 HUMAN TEETH

Age of donors	No. of teeth	No. of assays	d./m. ^{90}Sr/gm. tooth		
			Maximum	Minimum*	Average†
4	5	4	4·4	1·0	2·6 ± 0·6
6	6	3	4·7	0·2	2·1 ± 2·1
7	12	8	6·2	neg.	1·6 ± 0·8
8	17	7	3·2	0·1	1·5 ± 0·8
9 and 10	19	12	6·0	neg.	0·8 ± 0·4
11 and 12	11	9	2·3	neg.	0·8 ± 0·3
13 and 14	7	5	3·1	neg.	0·8 ± 0·2
15–18	5	5	1·4	0·2	0·8 ± 0·3
19 and 20	8	7	0·8	0·1	0·5 ± 0·3
21–30	17	11	1·8	neg.	0·5 ± 0·3
31 and up	14	10	1·3	neg.	0·4 ± 0·2

* Negative assays are those that counted equal to or less than reagent blanks.

† The standard 120-min. counting error is reported for the average assay.

d./m., Disintegrations/min.

A statistical analysis indicates that there is a definite inverse correlation between strontium-90 concentration and age. The significance test for linear correlation ($r = -0{\cdot}32$), based on 81 independent paired observations, reveals that the probability is less than 0·01 that this inverse relationship does not exist. The trend is expressed better, however, in an exponential form of the type :

$$S_c = B \exp(-kA)$$

where : S_c = strontium-90 concentration ; A = age ; B and k = constants.

The strontium-90 results for teeth are compared with those of bone in Fig. 1. The disintegrations/min. values were corrected to $\mu\mu$c./gm. calcium by assuming 40 per cent calcium in teeth. The trend is similar

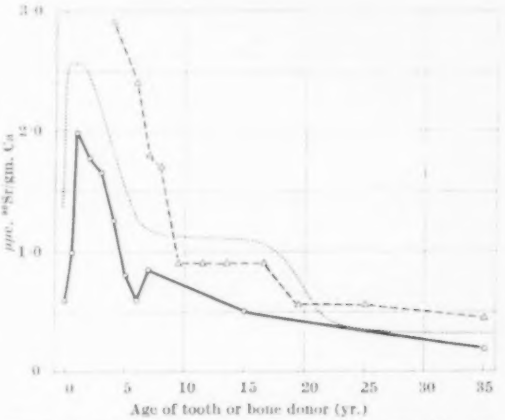

Fig. 1. Strontium-90 in teeth and bones. —△—, Strontium-90 in teeth, 1959 assays; ...., strontium-90 in bones, 1959, probable (Kulp); —○—, strontium-90 in bones,1958 assays (Bryant)

to the probable distribution of strontium-90 in Western man as reported by Kulp[1], and also to the results obtained by Bryant for bone collected in 1958[2,3].

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A New Effect of Ionizing Radiation on Nucleoprotein

AN aqueous solution of nucleoprotein, concentration 12 mgm./ml., prepared from calf thymus by the method of Kay, Simmons and Dounce[1], was irradiated with high-energy electrons to a dose of 4×10^6 rads. The dose was given in 4 min., and was assumed to be delivered to an oxygen-free solution, the initial 2 per cent of the dose using up all dissolved oxygen[2]. It was noted that immediately following irradiation a white suspension had been formed, and this afterwards collected at the bottom of the tube on standing. When the irradiated and control solutions were analysed it was found that in addition to producing a precipitate, irradiation had degraded amino-acids, purine and pyrimidine bases and deoxyribose sugar. Details of these degradations will be published else-

where: the present report is concerned with the nature of the precipitate.

No precipitate had been observed when calf thymus deoxyribonucleic acid (DNA) was irradiated under similar conditions[3]. The precipitate was not 'denatured protein' since no precipitate was formed when an aqueous solution of calf thymus histone was irradiated under similar conditions. It was possible that the precipitate could be 'cross-linked' material derived from both the protein and nucleic acid moieties. This possibility would be checked most suitably by irradiating a mixture of histone and DNA solutions. Unfortunately, mixing solutions of DNA (5 mgm./ml.) and histone (7 mgm./ml.) leads promptly to precipitation, presumably of a nucleoprotein complex[4]. As a substitute experiment, a solution containing histone and a mixture of deoxyribonucleotides was prepared and irradiated as described above. No precipitate was observed after irradiation, suggesting that cross-linking did not produce the precipitate obtained on irradiating nucleoprotein.

The most notable property of the precipitate obtained from irradiated nucleoprotein was its insolubility in water, *N* hydrochloric acid, *N* sodium hydroxide and 2*M* sodium chloride. The possible nature of the precipitate was discussed with Dr. K. S. Kirby, who suggested, in the light of his work with P. M. Frearson[5], that the precipitate was an acidic protein, and further that it may have small amounts of nucleotides attached to it. The precipitate was analysed as described here, and Kirby's predictions were confirmed. The precipitate contained an acidic protein with purine and pyrimidine bases attached, and so it is not derived from the bulk of the protein present (histone) in the nucleoprotein, but from a residual protein of the type originally described by Mirsky and Ris[6]. The production of this precipitate by ionizing radiation confirms the presence of an acidic protein in the structure of nucleoprotein. Further, in view of the possible role of the acidic protein in maintaining the structure of nucleoprotein[6], and as a site for enzymatic action[7], precipitation of the protein would affect profoundly the structure and function of the nucleoprotein in an irradiated cell.

Solutions of nucleoprotein, after irradiation, were spun, in a bench centrifuge, in the cold, and the clear supernatant solution decanted off. The precipitate was shaken in distilled water, and re-centrifuged. After washing five times the precipitate was freeze-dried. A weighed sample of the dried precipitate was hydrolysed in perchloric acid (72 per cent) at 100° C. for 1 hr. and analysed for phosphorus[8] and for purine and pyrimidine bases[9]. Large amounts of phosphorus were found (Table 1), and assuming it is present as phosphate, accounts for 70 per cent, by weight, of the precipitate. Small amounts of adenine, guanine, cytosine and thymine were found in the hydrolysate (Table 1). The base ratios were different from those of calf thymus DNA, amounts of guanine and cytosine being relatively greater (double) in the precipitate.

A second sample of the precipitate was hydrolysed in 6*N* hydrochloric acid, at 110° C. for 24 hr. and the hydrolysate analysed for amino-acids by two-dimensional paper chromatography. When the chromatograms were dipped into a solution of ninhydrin a large number of ninhydrin-positive spots appeared, their pattern being identical with that obtained when a sample of unirradiated nucleoprotein was analysed in the same way. The ninhydrin-positive spots were eluted and the amounts of amino-acids determined spectrophotometrically[10]. The relative amounts of amino-acids were similar to those for an unirradiated solution of calf thymus nucleoprotein except that the amounts of glutamic and aspartic acids were approximately 50 per cent greater in the precipitate than in the control. The total amount of amino-acids was approximately that given in Table 1, this value being the remainder when the weight of the purines and pyrimidines, as nucleotides, and of phosphorus, as phosphate, was subtracted from the weight of the precipitate.

Table 1. Analysis of Precipitate from Irradiated Nucleoprotein

		μM/mgm.
Bases:	Adenine	0·05
	Guanine	0·08
	Cytosine	0·07
	Thymine	0·03
	Total	0·23
Phosphorus		6·74
Amino-acids (molecular weight = 127)		2·2

The results obtained for the precipitate are consistent with Kirby's postulate[11] of an acidic protein attached to the nucleic acid moiety. The source of the large amounts of insoluble phosphate in the precipitate is not clear at present. It is Kirby and Frearson's experience that the acidic protein is insoluble and will remain in solution only when combined with DNA. If ionizing radiation severs the link between the acidic protein and the DNA, or breaks the DNA chain within a few nucleotides of the acidic protein, precipitation will promptly follow. There are two ways in which this can occur. Radiation can break the DNA chain, randomly along its length, and the acidic protein will be precipitated when breaks occur sufficiently close to it. In this case the *G*-value (molecules per 100 eV.) for formation of precipitate will be lower than the *G*-value for chain breaks by a factor which depends on how close to the protein a break needs to be for precipitation to occur. Alternatively, if energy introduced into DNA by ionization or excitation can migrate along DNA, as discussed recently by Prof. J. S. Mitchell[12], the migration will stop at the discontinuities which the acidic protein must represent in the regular structure of DNA. If the transferred energy is sufficient to break the nucleic acid chain, the acidic protein will be precipitated. If energy is readily transferred along the DNA, acidic protein will be precipitated by low doses of radiation.

Dounce[13] has recently discussed data which show that a residual protein is firmly bound to DNA, as first demonstrated by Mirsky and Ris[6]. While the nature of the binding has not been established, Kirby[14] and Dounce[13] have shown that the bonds are not ionic. Transition-group metals may be involved in a chelation-type bond between the acidic protein and the DNA (ref. 14), and the relatively large amounts of guanine are consistent with a bond of the type suggested by Kirby[14].

The amount of dried precipitate obtained was 0·5 mgm./ml. As 20 per cent of this is protein (see Table 1) the precipitate contains approximately 1·4 per cent of the total protein originally present. Before a *G*-value for formation of the precipitate can be calculated, it is necessary to determine how the yield of precipitate varies with dose, and also to obtain some estimate for the molecular weight of the acidic protein. Whatever the *G*-value may be, it is likely that this precipitation will play an important part in the biological effects of ionizing radiation, since it would alter so profoundly the structure and function

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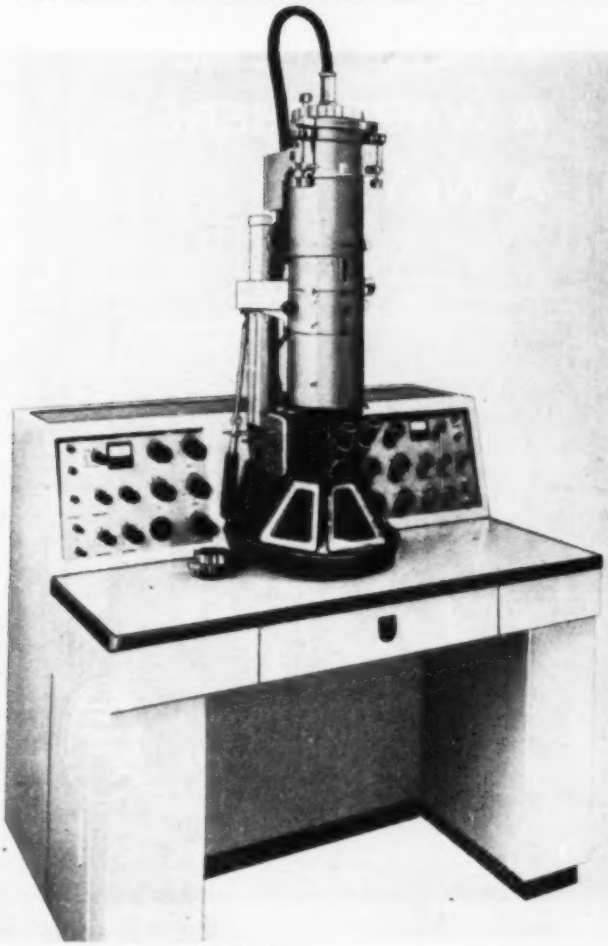

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of the nucleoprotein. Kaufman *et al.*[15] have studied several properties of nucleoprotein of onion roots, *Drosophila melanogaster* and calf thymus, before and after irradiation, and demonstrated degradation of the nucleoprotein with a few hundred r. of X-rays. More recently Hagen[16] has reported that whole-body irradiation of rats labilizes the thymus nucleoprotein. The precipitation described above is a possible mechanism for this labilization. Since Hagen obtained labilization with doses as low as 50 r., precipitation of the acidic protein would be an extremely radiosensitive reaction.

I am indebted to Dr. K. S. Kirby for his help in determining the nature of the precipitate. This investigation has been supported by grants to the Chester Beatty Research Institute (Institute of Cancer Research: Royal Cancer Hospital) from the Medical Research Council, the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service. Financial support was also granted by the William Shepherd Fund.

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'Nitric Oxide—and Oxygen Effect' in X-irradiated *Shigella flexneri*

In a number of cases, for example, bacteria and ascites tumour cells, it is known that nitric oxide increases radiation damage in anoxic conditions to a level comparable with that found in the presence of oxygen. The so-called oxygen effect is thus simulated by nitric oxide.

The starting point of the present investigations was the fact that the chemically very active gas nitric oxide has some effect on cell constituents, and the belief that this possibly, indeed probably, might become manifest after removal of free gas and subsequent X-irradiation. It appeared from the literature that the effect of an exposure of aqueous suspensions of bacteria to nitric oxide, followed by its removal prior to irradiation in oxygen-free nitrogen, had not been tested. While the present work was in progress, Howard-Flanders and Jockey[1] published results showing that this experiment had been carried out independently by them. However, their results obtained with the bubbling technique differ from the present ones obtained in a closed system in various respects not only in regard to the pre-treatment effect but also in some other points.

The results of the present series of experiments may be very briefly summarized as follows:

(*a*) Radiation sensitivity in the presence of nitric oxide is increased over that in nitrogen by a maximal factor of 3·2. A similar enhancement is found in oxygen and these results are in agreement with those of Howard-Flanders and Jockey.

(*b*) If the cells are pre-treated in nitric oxide for 30 min. at room temperature and irradiated in nitrogen after removal of free nitric oxide, sensitivity is again greater than in cells not pre-treated.

(*c*) Radiation sensitivity varies with the concentration of nitric oxide applied (up to a maximum value at 10 per cent nitric oxide in nitrogen), during or prior to irradiation. The minimal dose for 10 per cent survival is about 15 k.rads in the presence of the gas compared with about 20 k.rads after pre-treatment. For nitrogen controls this figure is 49 k.rads.

(*d*) Increasing duration of pre-treatment increases the subsequent radiation sensitivity.

(*e*) Cells kept in nitrogen (maximum period about 2 hr.) after pre-treatment with nitric oxide show a constant sensitivity.

(*f*) The pre-treatment effect is not due to residual free nitric oxide because of the evidence quoted in paragraphs (*c*) and (*d*) and also because of the high degree of consistency obtained for the radiation sensitivity in nitrogen.

The conclusion to be drawn from the present results is that the 'nitric oxide' effect seems largely caused by some latent, irreversible injury to unknown constituents of the cells with which nitric oxide may have combined. This injury is revealed on subsequent irradiation. The nitric oxide effect is thus different from the 'oxygen effect', which is only seen when irradiation occurs in the presence of the gas. Furthermore, the effect of time of contact with, and of the concentration of nitric oxide during, pre-treatment does not support the equivalence of nitric oxide and oxygen in their role in enhancing injury by radiation.

A detailed account of this investigation will be published in due course.

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Adaptation of a Chromatographic Technique for Autoradiography

A qualitative chromatographic technique has been previously described[1] which enables the investigation of simple compounds and their distribution in plant tissues to be accomplished without the immediate necessity of preparing extracts (for example, ether–water or alcohol). This method can be further extended by its use with radioactive isotopes and subsequent autoradiography.

Five day-old seedlings of *Phaseolus vulgaris* L., variety Improved Canadian Wonder (with radicles

approximately 4–5 cm. long) were injected with 10 µl. of a solution containing 0·4 mc./µl. of sucrose uniformally labelled with carbon-14. In one batch of seedlings (*a*) the sucrose was injected with a micro-syringe into the thickest part of the radicle, and in another batch (*b*) it was injected into the distal end (with respect to the embryo) of one of the cotyledons. The injected seedlings were then allowed to continue to grow normally, each batch being sampled at 1 hr., 2 hr., 4 hr., 1 day, 2 days and 4 days after injection. The sample seedlings were subjected to the chromatographic technique on Whatman No. 3 chromatography paper. After development, using conventional methods and solvents, the chromatograms were dried and placed with sheets of Ilford *G* X-ray film in cassettes and allowed to remain in contact with the films for 3–4 weeks. After this time, radioactive compounds were detected by developing the X-ray plate and could be compared with the compounds on the chromatograms after these had been treated with specific reagents (in this case, ninhydrin to detect amino-acids followed by benzidine–trichloracetic acid to detect the saccharides).

The results showed that in the case of the embryo-injected seedlings (*a*), the sucrose pool in the embryo became labelled and also the pool of reducing sugars, glucose and fructose. Various amino-acids were rapidly labelled and also (high molecular weight) material which did not move from the starting line of the chromatogram. Eventually, after four days, only small amounts of the labelled saccharides and amino-acids remained although considerable quantities of these compounds (unlabelled) were still evident on the chromatograms (that is, in the embryo). The majority of the radioactivity was found to be associated with the material at the starting line of the chromatogram. In the case of the cotyledon-injected seedlings (*b*), the cotyledon sucrose pool was labelled, but the evidence suggested that only amino-acids and 'high-molecular weight' material became further labelled; no reducing sugars became labelled. However, there is little reducing sugar in the cotyledons during germination (approx. 0·05–0·1 per cent dry wt.)[3].

In both cases (*a*) and (*b*), the labelled sucrose was found to appear in the other parts of the plant as well as in the injected part, but to a lesser extent in case (*a*) than case (*b*). This observation could possibly mean that sucrose can be translocated in both directions in the plant (that is, cotyledons to embryo and vice versa); this is consistent with the findings of Rabideau and Burr[3], of Chen[4], and of Palmquist[5] who observed that solutes can be translocated in both directions in the stems of *P. vulgaris* and other plants. Nevertheless, the net flow of sucrose was in the direction cotyledons to embryo as would be expected.

In case (*b*), injected cotyledons, as well as the labelled sucrose which appeared in the embryo, labelled glucose and fructose appeared in the reducing sugar pool of the embryo. This could be consistent with the fact that an invertase (optimal activity at *p*H 5·0) can be extracted from this part of the plant at these stages of germination (ref. 2 and Cooper, R. A., and Greenshields, R. N., unpublished results, 1960).

It is proposed in future work to inject other carbon-14 containing compounds into this plant, for example, galactose-^{14}C and raffinose-^{14}C, to determine the fate of these compounds on germination. The raffinose family of oligosaccharides (namely, verbascose, stachyose, raffinose and sucrose) occur in this plant[6] and rapidly disappear on germination, leaving only sucrose in the cotyledons and sucrose, glucose and fructose in the embryo (that is, no galactose)[3]. Thus the fate of the galactose might be determined.

Although effects due to 'cut-respiration'[7] cannot be overcome, because the pattern and changes of the saccharides in untreated plants is the same as in treated plants, the effects due to 'cut-respiration' are probably very small. Furthermore, in the case where injected radioisotopes are translocated to other parts of the plants, for example, sucrose appearing in the embryo after injection in the cotyledons, 'cut-respiration' would not complicate the interpretation of the results.

Thus it can be seen that this technique might provide a useful tool in helping to solve translocation problems and also to indicate possible reactions that occur *in vivo*. Although purely qualitative, the technique indicates lines along which quantitative work might be pursued.

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Effect of *p*H on the Sensitiveness of Trypsin to Ionizing Radiation

Although oxygen usually increases the sensitivity of biological systems to ionizing radiations, it was found that with the enzymes chymotrypsin[1] and trypsin[2], in dilute aqueous solutions, the presence of air as compared with vacuum diminished the sensitiveness by a factor of about 3. In these experiments the enzyme was dissolved in 10^{-3} *N* hydrochloric acid, in which it was believed to be most stable. We have now, in the case of trypsin, examined the effect of varying the *p*H of the solution in which it is dissolved and find that the effect of oxygen is markedly dependent on the *p*H. Some typical figures of the specific inactivation dose to 220-kV. X-rays are given in Table 1 (in rads/gm./ml.).

Table 1

Solvent	0·1 *N* HCl	0·01 *N* HCl	0·001 *N* HCl	Water
*p*H (approximate)	1	2	3	6
$D_{0.5}$/c. in air ($\times 10^{-5}$)	0·3	1·0	1·5	1·0
$D_{0.5}$/c. *in vacuo* ($\times 10^{-5}$)	0·25	0·4	0·6	1·0

It can be seen that the difference between the sensitiveness *in vacuo* and in the presence of air is a maximum at about *p*H 3 and diminishes both in more and in less acid solutions. Increasing the chloride ion concentration without changing the *p*H had little effect.

In order to explain this behaviour we must consider the reactions:

$$H + O_2 \rightarrow HO_2 \quad (1)$$

$$HO_2 \rightarrow H^+ + O_2^- \text{ (}pK\text{ between 2 and 3) (ref. 3)} \quad (2)$$

$$H_2 \rightarrow H^+ + H \text{ (}pK\text{ between 1 and 3) (ref. 4)} \quad (3)$$

It can be seen that at $p\mathrm{H} > 3$ (approximately) HO_2 will be present under equilibrium conditions mainly as O_2^-, which, like H, is a reducing agent. In so far as we are concerned with oxidation-reduction effects, no great change will be brought about by the presence of oxygen. At $p\mathrm{H} < 3$, HO_2, which is an oxidizing agent, will be present in an undissociated form, and it is evident that this is less effective than H or O_2^- in causing inactivation of the enzyme. At still lower $p\mathrm{H}$ (~ 2), the formation of H_2^+ begins to be effective, and in this region there will be a competition between H^+ and O_2 for the available H radicals, so that the amount of HO_2 will be diminished. As H_2^+, like H, is a reducing agent, it follows that the effect of oxygen may be expected to be diminished again at low $p\mathrm{H}$.

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BIOLOGY

Survival of Cutaneous Homografts after Transplantation of Lymph Nodes immunized against the Host

Up to now, two main experimental methods have been established to overcome tissue incompatibility in genetically different individuals. One of them is the acquired tolerance in embryogenesis or shortly after birth[1,2], and the other consists in X-ray irradiation of the host with the lethal dose and a life-saving bone-marrow transplantation[3].

In this communication I should like to demonstrate a new approach to overcome tissue incompatibility by influencing the regional lymphatic system with the transplantation of lymph nodes immunized against the host.

I have experimented on rabbits (chinchilla and albino breed) weighing 2,000–2,500 gm. Experiments were performed on three groups within one year. Each group comprised 15 rabbits, five of them being recipients of skin (rabbit *A*, chinchilla), 5 donors of nodes immunized against the recipient (rabbit *B*, albino) and 5 donors of skin (rabbit *C*, albino) (Fig. 1).

From the left ear of the future recipient (*A*) a skin flap 2 cm. × 2 cm. was grafted on the ear of the lymphatic node donor (*B*). One week after the skin graft I extirpated the lymph node from the collecting area of the ear, cut it in thin slices and transplanted it subcutaneously into the base of the recipient's ear (*A*) and, at the same time, grafted the skin of the donor's ear (*C*) on that site.

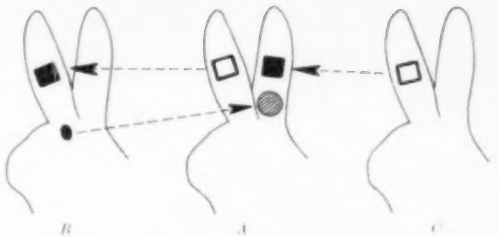

Fig. 1

I have studied the survival of the graft only macroscopically because it differed in colour from the skin of the host. I assessed the result statistically with a t test against the control groups in which I simultaneously transplanted on host *A* the node without antibodies against the host and a graft from donor *C*.

The results are summarized in Table 1. In all cases I was able to achieve a statistically extraordinary long survival-rate of the graft. In controls, the graft was rejected between the eighth and the thirteenth day. In the groups after treatment of the regional lymphatic system of the host by antibodies against the host with a transplanted regional lymph node the grafts were rejected in twelve cases between the fifty-fourth and the eighty-sixth day. In three rabbits the graft survived practically permanently.

Table 1. Survival-Rate of Skin Homografts on a Rabbit's Ear

Control group	Influencing of the host with antibodies against the host		Control group	Influencing of the host with antibodies against the host
8	54		12	70
8	58		12	70
9	62		12	79
10	62		12	86
10	63		13	187 (+)
10	67		13	450 (still alive)
11	69		13	746 (still alive)
11	70			
Average:	10·9 ± 0·3	average of the first 12 animals	67·5 ± 2·5	

In one rabbit from the first group, the graft has survived to this day, that is, two years since November 1958 (Fig. 2). In another rabbit from the second group the graft survived macroscopically for six months in perfect condition before the rabbit died of pneumonia. A third graft from the last group is surviving in one-quarter of the original graft for almost one year now in a good condition, that is, since December 1959.

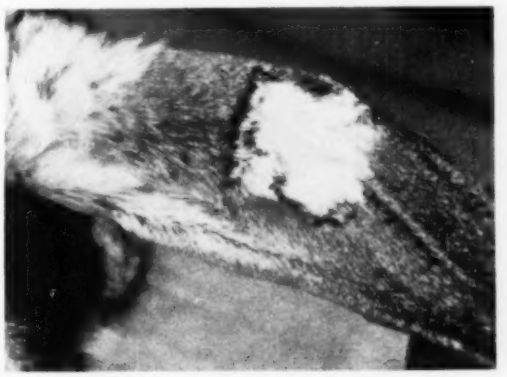

Fig. 2. A homograft two years after the transplantation

The importance of the lymphatic system for achieving transplantation immunity has been differently interpreted in the literature. While the majority of papers stress the changes of the regional lymphatic system after homografts[4] there are also papers categorically denying its importance[5]. In an earlier paper I have attempted to point out the importance of the regional lymphatic system in establishing transplantation immunity. After extirpation of the regional lymphatic system or its destruction by means of *TS* 160 (nitrogen mustard), the survival-rate of the graft could be prolonged for 15–65 days[6].

The results of treatment of the regional lymphatic system with antibodies against the host seem to be important for a new approach to overcome tissue incompatibility.

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A Method of determining Embryonic Orientation in the Hen's Egg

I wish to report a successful attempt at detecting embryonic position in the hen's egg using, so far as it is known, a previously untried technique. It consists of X-raying the incubated egg to determine the skeletal morphology of the embryo. With the egg held in a horizontal position the embryo's longitudinal position can be easily detected. On rotating the egg through a 90° angle, exposing it a second time, and then viewing the X-ray plates in the order of taking, the direction in which the head is turned can be accurately determined.

In this way, not only can the normal orientation of embryos be studied but also the lethal nature or hatchability of certain conventional malpositions about which controversy[1] has arisen in the past, since the technique does not involve the death of embryos.

Fig. 1 shows the normal position adopted by embryos approximately 36 hr. before hatching is completed; the long axis of the embryo coincides with that of the egg and the head and beak are turned to the embryo's right across the breast towards the broad end of the egg and in close proximity to the air cell (clearly defined dark area). In Fig. 2 the longitudinal position of the embryo is reversed so that the head is seen towards the small end of the egg away from the air cell, into which it is normal for the embryo's beak and head to enter during the process of hatching.

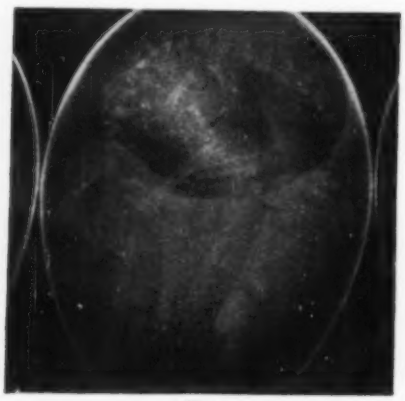

Fig. 1

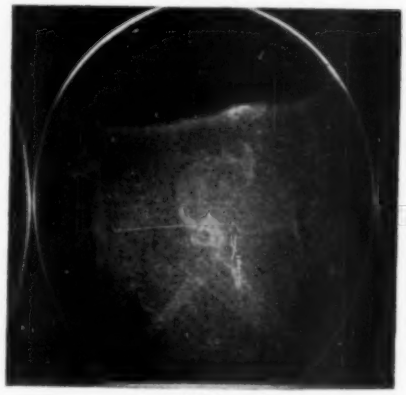

Fig. 2

Detailed results of this work will be reported in the near future; but, for the present, work has shown that (*a*) the head-between-thighs position of malposition I should be regarded as a transitional stage in the normal orientation of embryos to the hatching position rather than a cause of death or failure to hatch, and (*b*) embryos adopting malposition II (head in the small end) or malposition III (head to left) have, respectively, a slightly better than one in two and one in five chance of hatching.

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Effect of Temperature and Grafting on Vegetative Growth Phases of Algerian Ivy

The closely similar English and Algerian ivies, *Hedera helix*, Linn. and *Hedera canariensis*, Willd., do not flower until the juvenile vining type of growth changes into a stiff erect form. This mature type of growth has entire, ovate to lanceolate leaves, and the round stems rarely produce aerial roots. The juvenile trailing stems are somewhat flattened, frequently produce aerial roots, and the leaves are palmately lobed. Both stems and petioles frequently have red pigments. Doorenbos[1] was able to produce many reversions to the juvenile form by grafting the mature fruiting form of English ivy on juvenile two- or three-year seedlings or on juvenile plants grown from cuttings. Plants of adult ivies grown on juvenile understocks for approximately a year outdoors in a lath house in the relatively cool coastal climate of west Los Angeles did not exhibit the reversions described by Doorenbos. Preliminary experiments indicated that mature budded plants on juvenile understocks all reverted to the juvenile form when grown for more than a year at 80° F. but produced few reversions at lower temperatures.

Table 1. Growth Responses in Three Environments

Environment	Total plants observed	Plants with adult characters	Plants with juvenile characters	Total No. of shoots	Average shoot length (cm.)
Lath house	66	45	21	155	23·55 ± 1·04
Glasshouse, 60° F.	60	51	9	165	24·45 ± 1·18
Glasshouse, 80° F.	60	0	60	96	25·94 ± 1·52

Closely similar results were obtained in a more extensive experiment started on February 19, 1959, using budded plants of Algerian ivy. The plants were distributed among the three environments on April 20. The glasshouses were air conditioned with automatic controls. On May 4 the natural buds of the stocks were excised to force growth from the inserted buds. On September 14 the plants in both the lath house and the 60° F. glasshouse were predominantly adult and were showing flower buds, but in the 80° F. glasshouse the growth was largely juvenile. The plants were headed back on September 29 to about 6 in. above the bud union. Final results were taken on November 16 and are shown in Table 1. The highest temperature did not increase the length of shoots appreciably, reduced the number of shoots, and promoted reversions to the juvenile type of growth. During this experiment, 26 own-rooted, cutting-grown plants of the mature form of the same clone were kept in each of the same three environments. No changes in type of growth occurred, except that in the glasshouse kept at 80° F. two plants produced shoots with some juvenile characters. On own-rooted mature plants, reversion shoots occasionally appear and are nearly always produced close to the level of the soil.

The amount of mature scion wood initially in the graft combination also influenced the responses. This was demonstrated in an experiment with a clone of Algerian ivy grafted or budded on a juvenile clone of the same species. The plants were started on August 24, 1959, and were placed in the three environments used in the preceding experiments. Buds were excised from the understocks on November 17 in order to force top growth. Growth of the plants in the lath house was slower, but the shoot growth was closely comparable in the two glasshouses. The plants were classified on March 25, 1960. The results are shown in Table 2. These responses show that the greater quantity of the mature type of wood on the scion in grafting diminished the reversions to juvenile growth.

Juvenile scions on mature understocks were also tested. Forty-two grafts, potted on November 17, 1958, were kept in a glasshouse at 60° F. On June 1, 1959, none of the scions had produced any growth which was not fully juvenile. The influence of temperature has been noted in a few other plants. Hudson and Williams[3] noticed that high temperatures favoured the production of the juvenile leaf type on raspberry shoots, and Njoku[4] found a similar relationship in *Ipomoea*, as did Fisher[2] on *Ranunculus*.

Table 2. Responses of Shoots on Budded and Grafted Plants in Three Environments

Treatment	80° F.		60° F.		Lath house	
	No. of plants	No. juvenile	No. of plants	No. juvenile	No. of plants	No. juvenile
Budded	73	71	96	14	77	1
Grafted	106	27	101	3	103	0

These experiments confirm the observations of Doorenbos, but also show that reversions to the juvenile form are influenced by temperature and also by the amount of mature tissue present in the graft combinations initially.

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BACTERIOLOGY

Isolation of Lysozyme-soluble Mucopeptides from the Cells Wall of *Escherichia coli*

The cell walls of the Gram-positive bacteria have been shown by Salton[1] and by Cummins and Harris[2] to consist mainly of polymers, later termed mucopeptides, containing a limited number of amino-acids (usually four), two amino-sugars and sometimes one or more hexoses. Two of the amino-acids, alanine and glutamic acid, are, at least partly, in the D-form. This, together with the occurrence of muramic acid, and sometimes of diaminopimelic acid as well, distinguishes mucopeptides from other types of macromolecule. A further characteristic is sensitivity to lysozyme. The mucopeptides from some bacterial species are completely digested by this enzyme, and all appear to be attacked slightly[3]. The synthesis of mucopeptide in washed suspensions is inhibited by penicillin[4,5].

The cell walls of the Gram-negative bacteria are much more complex (see Salton[6]) and contain a good deal of protein and polysaccharide. However, the presence of mucopeptides similar to those of the Gram-positive bacteria was indicated by the fact that Gram-negative cells could be lysed by treatment with lysozyme[7], and that penicillin produced osmotic fragility in *E. coli*[8]. In addition, when walls of *E. coli* were treated with lysozyme, soluble fragments were recovered containing the characteristic components of mucopeptide, namely, diaminopimelic acid, muramic acid, glucosamine, alanine and glutamic acid[9]. The object of the work to be described was to separate the mucopeptides of *E. coli* sufficiently from protein and polysaccharide to allow its composition and some of its properties to be examined. The procedure finally adopted was as follows.

The bacteria (about 10 gm. dry weight) were broken by shaking with Ballotini beads in a Mickle disintegrator, and the walls sedimented at 10,000*g*. The sediment was suspended in water and heated at 100° C. for 30 min. to destroy any lytic enzymes that might have been present. All further procedures were carried out at room temperature unless otherwise stated. The crude wall preparation was then extracted three times with ethanol/ether (3 : 1) and then with other. The residue was dried in air, and treated for the reduction and alkylation of disulphide bonds[10] in the protein by suspending the powder in 10 *M* urea

Table 1. Molar Ratios of Amino-acids and Hexosamines in the Cell-wall Mucopeptides of *E. coli* and Micrococci

Strain	Glutamic acid	Alanine	Serine	Glycine	Lysine	**DAP	GM*	Mur.†
E. coli								
W	1·0	1·5	0·13	—	0·19	0·70	0·80	0·51
M	1·0	1·5	0·16	—	0·21	0·67	0·70	0·47
B	1·0	1·5	0·13	—	0·22	0·74	0·76	0·43
K 12	1·0	1·4	0·15	—	0·20	0·63	0·80	0·50
ML 30	1·0	1·5	0·14	—	0·23	0·70	1·0	0·90
Micrococci								
524/*SC*	1·0	1·8	—	3·2	0·6	None	1·0	1·1
H	1·0	3·2–3·7	—	—	0·9–1·2	,,		
Duncan	1·0	2·8	—	6·3	1·9	,,		
11	1·0	1·4	—	0·05	0·5	,,		
Oxford	1·0	1·9	—	4·9	1·0	,,		
M. lysodeikticus	1·0	1·9–2·5	—	1·2–1·6	1·0	,,		

* GM = glucosamine; **DAP = diaminopimelic acid.
† Mur. = muramic acid. Both hexosamines are *N*-acetylated in *S. aureus* and are presumably so in *E. coli*, although this has not been determined. The molar ratios for coliform mucopeptides were determined as previously described (ref. 13). The values for strains of micrococci are those quoted by Rogers and Perkins (ref. 11).

(50 ml.) containing mercaptoethanol (1 ml.). After several hours, excess iodoacetic acid was added, and the product washed well and digested overnight at 35° C. with pepsin (20 mgm.) in *N*/20 hydrochloric acid. The product still contained more than 50 per cent protein. To remove this, it was extracted three times with 90 per cent formic acid (20 ml.) and twice with 90 per cent phenol (20 ml.). Finally, the residue was extracted three times with 10 ml. of copper ethylenediamine (6 per cent copper hydroxide and 8 per cent ethylenediamine) and washed several times with *N*/20 hydrochloric acid to remove copper. Although some mucopeptide was always lost at this stage, the extraction removed mainly protein and polysaccharide.

After drying with acetone and ether, a white powder was obtained representing about 1 per cent of the bacterial mass, and containing the following major constituents: diaminopimelic acid, lysine, serine, glutamic acid, alanine, glucosamine and muramic acid. Together these accounted for 75–80 per cent of the total material. In addition, chromatography of acid hydrolysates revealed the presence of small amounts of all the other amino-acids characteristic of protein, and these together represented a further 10 per cent. The remainder of the preparation consisted of unidentified carbohydrate.

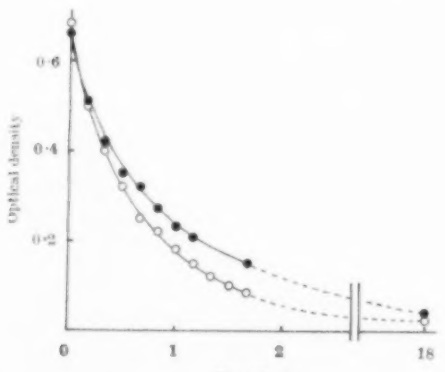

Fig. 1. Digestion of mucopeptides prepared from *E. coli B* and *M. lysodeikticus* by lysozyme. The mucopeptides were suspended at a concentration of 1·5 mgm./ml. in 0·1 *M* phosphate buffer (pH 6·0) and incubated with lysozyme at room temperature. Optical density at 620 mμ was measured at intervals. ○, Values for *M. lysodeikticus* in the presence of 10 μgm./ml. lysozyme; ●, values for *E. coli* mucopeptide, in the presence of 100 μgm./ml. lysozyme. This high concentration of lysozyme was necessary because the mucopeptide from *E. coli* contained an inhibitor of the enzyme apparently introduced during preparation (see text)

To determine whether the method of extraction was likely to damage the mucopeptide, the whole procedure was applied to Gram-positive mucopeptides. The end-product was found to be identical with that obtained by the more conventional methods.

Table 1 shows that the mucopeptides isolated from the five strains of *E. coli* so far examined are virtually identical, and the relative proportions of glutamic acid, alanine, and glucosamine are similar to those found in the mucopeptide of *Staph. aureus* 524. These values, and those for mucopeptides from four other strains of micrococci (see Rogers and Perkins[11]), have been included. It is apparent that, in the latter group, there is much more variability, and an even greater scatter has been found in the walls of lactobacilli[12].

The mucopeptides from *E. coli* were examined for sensitivity to lysozyme, and found to contain an inhibitor of the enzyme probably introduced in the preparation. 1 mgm. of mucopeptide contained sufficient inhibitor to inactivate 10–20 μgm. of lysozyme. However, if sufficient enzyme was added to overcome the inhibiton, there was rapid digestion of the mucopeptide accompanied by a fall in optical density of more than 90 per cent. This is similar to the reduction in optical density found with the mucopeptide of *Micrococcus lysodeikticus* (see Fig. 1).

It thus appears that the cell walls of *E. coli* contain a mucopeptide which, in its composition and its sensitivity to lysozyme, resembles those of the Gram-positive bacteria. The main difference seems to be that whereas the latter have been found to contain either diaminopimelic acid or lysine, the coliform mucopeptides contain both. This conclusion is supported by the fact that lysine increases proportionately with the diaminopimelic acid at each stage of the purification.

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ENTOMOLOGY

A Species of *Tetranychus* Dufour (Acarina) from Uganda

Recently, Baker and Pritchard[1] described certain tetranychoid mites from Africa, among which they listed *Tetranychus cinnabarinus* (Boisd.) and *T. telarius* (L.). Their work embraced a study of preserved material from Namulonge, Uganda, which they ascribed to the former species. The two species mentioned, together with others, have for long been the subject of controversy and have been included in the '*telarius* complex' by authors.

Boudreaux[2] produced evidence, from Nearctic specimens, of a series of constant morphological differences in both males and females whereby the components of the '*telarius* complex' could be separated. Baker and Pritchard applied his principles to their Ethiopian material. Thus the adult female of *T. cinnabarinus* is said to possess lobes on the dorsal integumentary striæ of the hysterosoma which are all semicircular or triangular (Fig. 1, enclosed by circle), whereas those of *T. telarius* are said to be mostly wide (Fig. 1, enclosed by square). Fig. 1 is a photograph of the dorsal integument of the hysterosoma of a typical adult female (feeding stage) of a species of *Tetranychus* commonly found on cotton at Namulonge. With this mite it is possible to follow the series of keys of Baker and Pritchard as far as couplet 9 in the key to species of *Tetranychus*; but at this point neither the name *T. cinnabarinus* nor *T. telarius* can be applied to it since it apparently possesses the integumentary characters of both species. The portion of integument figured displays 80 semicircular or triangular lobes and 30 wide ones; thus neither are they wholly of the former type nor mostly of the latter.

The conformation of the apex of the ædeagus of males of the Namulonge species presents a further anomaly. Baker and Pritchard, again following Boudreaux, described the apex of the ædeagus of of *T. cinnabarinus* as having a somewhat rounded anterior development, an angulate dorsal margin and an axis which forms a slight angle with the axis of the shaft. The drawing which accompanied their description agrees closely with Fig. 2 presented here (type *A*). On the other hand, *T. telarius* is said to have an ædeagus with the anterior development acute, the dorsal margin rounded and the axis parallel to that of the shaft. Fig. 3 represents this type of ædeagus (type *B*). However, Figs. 2 and 3 are photographs of two males of the Namulonge species which were born on the same day of the same female parent, by arrhenotokous parthenogenesis. The female, a typical adult (such as that described above) was isolated on emergence from the deutonymph and the male progeny produced were themselves reared in isolation. Apart from the morphology of the ædeagus, both mites were identical so far as could be observed. Since haploid males are produced in arrhenotoky, it is tempting to assume that ædeagi of types *A* and *B* appear as a result of a simple segregation of the members of a pair of allelic characters in the female, but insufficient material has been examined to establish the ratio in which the two types occur, nor is it possible to state unequivocally that no intermediate form is found.

It is concluded that the means evinced by Boudreaux for the micromorphological separation of the components of the '*telarius* complex' may not be readily applied to all Ethiopian forms before a comprehensive study of the living material has been undertaken.

Specimens figured here were mounted from life in Hoyer's medium, photographed by Zeiss phase-con-

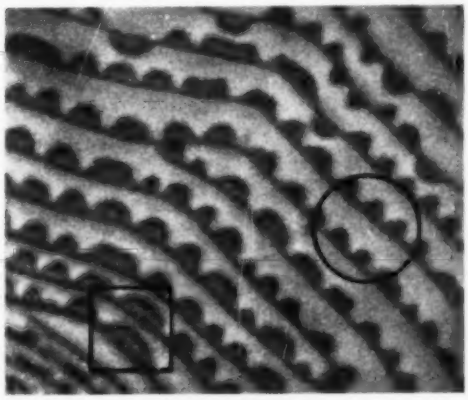

Fig. 1. Dorsal integument of adult female in region of right anterior dorsocentral hysterosomal seta

Fig. 2. Lateral view of ædeagus of adult male, type *A*

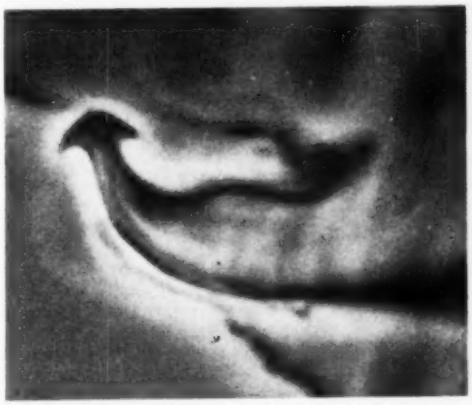

Fig. 3. Lateral view of ædeagus of adult male, type *B*

trast apparatus at 1,000 diameters and afterwards enlarged to 3,750 diameters.

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VIROLOGY

Centrosema Mosaic: a Plant Virus Disease transmitted by both Aphids and Plant Bugs

Investigations have been carried out in Papua and New Guinea on a previously undescribed virus disease, *Centrosema* mosaic, which infects several tropical legumes.

The virus is transmitted mechanically, by *Cuscuta campestris* Yuncker, by two aphid species, *Brachycaudus helichrysi* (Kltb.) ? variety *warei* Theob. and *Aphis gossypii* Glov., and by two species of plant bugs of the genus *Nysius* (Table 1).

Table 1. Insects Capable of Transmitting *Centrosema* Mosaic Virus to *Crotalaria anagyroides* H.B.K.

Insect	Insect form	No. of insects per plant	Proportion of plants infected
Aphididae			
Brachycaudus helichrysi var. *warei*	apterae	10	20/20
Aphis gossypii	apterae	10	6/20
Lygaeidae			
Nysius sp. (green)	winged	20	10/60
Nysius sp. (brown)	winged	20	38/60

It is not usual for a plant virus to be transmitted by both an aphid and a plant bug. *B. helichrysi warei* is able to transmit *Centrosema* mosaic after an access feeding period of 12 min. and remains infectious for 48, but not for 72 hr.; pre-access starvation increases the efficiency of transmission. These facts suggest the virus is transmitted in a non-persistent manner[1]. Winged females, wingless females and first and second instars of *B. helichrysi* var. *warei* are all capable of transmitting the virus.

Though *Aphis gossypii* can transmit the virus under laboratory conditions, it is probably not a natural vector as it has not been recorded feeding on *Crotalaria* spp. or *Centrosema pubescens* Benth., in the field.

Nysius spp. are able to transmit *Centrosema* mosaic to *Crotalaria anagyroides* after an access feeding period of 2 hr. and within a test feeding period of 24 hr.

The virus naturally infects and produces mosaic symptoms on *Centrosema pubescens*, *Crotalaria anagyroides*, *C. goreensis* Guill. and Perr., *C. retusa* L., *C. mucronata* Desv., *Calopogonium mucunoides* Desv. and *Desmodium distortum* (Aubl.) Macbride. The virus can also be mechanically transmitted to *Crotalaria juncea* L., *C. spectabilis* Roth., *C. incana* L., *C. intermedia* Kotschy, *C. lanceolata* E. Mey., and *C. usaramoensis* Baker F., and produces mosaic symptoms in all these hosts. *Stizolobium deeringianum* Bort. exhibits a pale greenish-yellow chlorotic spotting of the first set of trifoliate leaves following inoculations of the first true leaves with infective sap; subsequent leaves show mosaic symptoms which are systemic and persistent. The virus failed to infect *Phaseolus vulgaris* L., *P. mungo* L., *P. aureus* Roxb., *P. lunatus* L., *P. calcaratus* Roxb., *Vigna sinensis* (L.) Savi, *V. unguiculata* (L.) Walp., *Vicia faba* L., *Pisum sativum* L., *Medicago sativa* L., *Canavalia ensiformis* DC., *Datura stramonium* L., *Nicotiana tabacum* L., *N. glutinosa* L., *Lycopersicum esculentum* Mill., *Petunia hybrida* Vilm., *Cucumis sativus* L., or *Chenopodium amaranticolor* Coste and Reyn. following mechanical inoculation. The virus is inactivated after an exposure of 10 min. at 58° C.; at a dilution of 1 in 2,000, and after an exposure of 6 hr. at a room temperature of 28° C.

Further details of these investigations will be published elsewhere.

We acknowledge with appreciation the identification of the insect vectors by Dr. V. F. Eastop of the British Museum, and help given by Dr. M. F. Day of the Commonwealth Scientific and Industrial Research Organization, Canberra.

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GENETICS

A Dominant Gene for Renal Adenomas in the Rat

Familial renal adenomas in the rat have been described in a previous report[1]. They usually occurred as multiple tumours and were bilateral. The tumours were simple cysts, papillary cystadenomas, solid eosinophile adenomas or solid basophile tubular adenomas. They varied in size from barely visible to large growths which included almost the entire kidney (Fig. 1). The material consisted of a number of individuals from a line of Wistar rats maintained in this laboratory, indicating that the condition was genetically controlled.

The breeding of these animals is a laborious process as they have to be opened and inspected to determine the presence of tumours. Males are inspected through a mid-abdominal incision while the kidneys of females are inspected through dorsolateral incisions as they frequently failed to care for their litters after abdominal operations. Furthermore, although

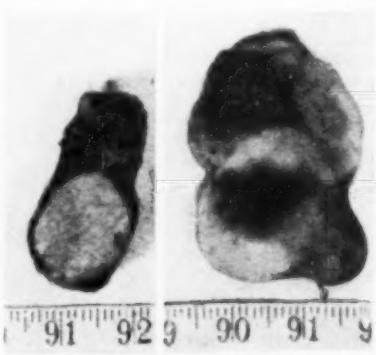

Fig. 1. Longitudinally bisected left and right kidneys of a female with large bilateral tumours

tumours have been found macroscopically in rats as young as five months, they are not usually readily detectable until 10 or 12 months of age, and even then only as small cysts which later develop into solid tumours.

The genetic analysis was begun with a single-tumour male, one of a litter of six, three of which were normal and three had tumours. The mother was tumour-bearing and the father normal. This male was outcrossed to six albino females from a closed laboratory population after having failed to produce any offspring with his three sisters.

A total of 106 F_1 animals was obtained from this outcross, 64 ♀♀ and 42 ♂♂. The inspection and microscopic examination of this first generation have been completed.

A complete post-mortem examination was made on all the F_1 animals, including microscopy of a number of organs, especially the lungs. The types of renal tumours observed are the same as those previously described. In some of them the microscopic picture resembles carcinoma with atypia of the cells and apparently invasion of the surrounding renal tissue. No invasion of the blood vessels has been observed, however, and no metastases have been found in any of the animals in spite of careful examination. The skeleton has also been examined by X-rays in some animals with large tumours, with negative results.

Seventeen of the F_1 animals died too young to be included in the material, leaving a total of 89 F_1 progeny. These were killed or died at ages varying from 19 to 24 months, and the kidneys of all were examined microscopically. All the animals classified as tumour-bearing were verified histologically. One animal macroscopically classified as normal was found to have an incipient tumour on microscopic examination: otherwise there was complete agreement between the macroscopic and the microscopic diagnosis. The results of this classification are presented in Table 1.

Table 1. Histological Diagnosis of Renal Adenoma in F_1 Progeny from a Single Tumour-bearing Male outcrossed to Six Unrelated Females of a Different Strain

	Tumour	Normal	Tumour (per cent)
	♀♀ 22	31	41·5
	♂♂ 15	21	41·7
Total	37	52	41·6

This is fairly close approximation to a 1 : 1 ratio.

In order to eliminate the possibility that there might be genetic factors involved in tumour development in the albino strain from which the mothers of the first generation were derived, one of the F_1 tumour males was outcrossed to 20 females of an entirely unrelated strain of hooded rats. Although the examination of all these progeny is not complete, the numbers are sufficiently large to confirm the correctness of the assumption that a single dominant gene determines the development of the tumours. These animals have not yet been examined histologically but the preliminary results of macroscopic examination of 113 progeny from this outcross are: 13 tumours, 19 cysts, 31 doubtful and 50 normal. In this case the sire is known to be a heterozygote, while the original sire of the F_1 might have been a homozygote as it was not possible to trace its ancestry with sufficient accuracy to eliminate the latter possibility.

An F_2 has been obtained by crossing inspected F_1 tumour males to F_1 females which had not yet been inspected. As the tumour females produce few and small litters, only 20 F_2 rats from such matings have so far been inspected at ages of 10–15 months, revealing 4 tumours, 4 cysts, 5 doubtful and 7 negative. This is a somewhat higher ratio of tumour animals than in F_1, but the material is still too small to calculate any ratios, and it is not yet known whether the homozygote is viable.

No correlation has been found between tumour development and sex, nor does there seem to be any influence of number of pregnancies on tumour development in females. The tumours in the F_1 animals were graded for number and size to determine whether there was any correlation between grade and sex; but the results were negative.

Further experiments are being carried out to determine the pathogenesis of the tumours.

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HISTORY OF SCIENCE

Origins of the Copernican Revolution

The results of the 'Copernican Revolution' have been well described by historians of science. Less has been said about the origins of this revolution; that is, the problems and facts leading Copernicus to a conviction of the physical truth of the Earth's daily rotation and of its annual revolution around the Sun. I have developed a conjecture on this problem which will doubtless prove incorrect when closer study of the relevant sources is made, but which at least directs attention to a natural series of scientific problems, and which is based on Copernicus's own recollections of his early work.

Rheticus, the disciple of Copernicus in the latter's old age, gave in his *Narratio Prima*[1] a list of six principal reasons "why we must abandon the hypotheses of the ancient astronomers". The form of these ensures that they were taken from Copernicus himself. Of the six, the third, fourth and fifth have no surprises, relating to apparent planetary distances, uniform circular motion and economy, respectively. The sixth invokes the rule "that the order and motions of the heavenly spheres agree in an absolute system" and cites the non-observance of this rule by earlier astronomers as a cause of the bad state of the astronomy of the time. The first and second reasons must be quoted in full:

"In the first place, the indisputable precession of the equinoxes, as you have heard, and the change in the obliquity of the ecliptic persuaded my teacher to assume that the motion of the earth could produce most of the appearances in the heavens, or at any rate save them satisfactorily.

"Secondly, the diminution of the eccentricity of the sun is observed, for a similar reason and proportionally, in the eccentricities of the other planets".

These 'reasons' indicate that Copernicus was not exclusively concerned with the problem of short-range predictions of the planetary positions, although this is the only part of his work which has been popularized by historians. Further evidence for a concern with long-term variations comes in the prefatory letter of the *De revolutionibus*. There, first in his list

of reasons for thinking of a new method for astronomy, is: "the mathematicians are so unsure of the movements of the sun and moon that they cannot even observe or explain the length of the seasonal year"[2].

It was almost universally believed, from early Islamic times to the sixteenth century, that both the rate of precession (motion of the fixed stars in longitude) and the length of the year were variable. Other parameters of basic astronomical theory were also considered variable (see the foregoing reasons), but I do not take them into account in my present work. A full understanding of these variations was considered necessary for any long-term prediction of the planetary positions, or of eclipses, and for calendar reform. This last was not a trivial task, for one cannot get the true mean of a quantity of unknown variation by averaging over an arbitrary interval. Moreover, the Christian calendar is lunar as well as solar, because of the definition of Easter; this made the problem more delicate. An important part of Copernicus's work was the institution of method in the study of these problems, which had not been treated by Ptolemy. It was for his achievements in these problems that he was called "the restorer of astronomy" by such later astronomers as Clavius. In actual fact, both the precession and the length of the year are constant, and both pseudo-problems died suddenly at the end of Copernicus's century. This is one cause for their neglect by historians. The other is that, from Galileo onwards, debate was centred on the physical and cosmological implications of the Copernican system rather than on the details of his mechanisms.

In my conjecture, I use the 'reasons' as indications of problems, and take a (supposedly) hard fact from the *Commentariolis*[3], written by Copernicus early in his career. This is, that from past records it appears that while the equinoctal year is variable, the sidereal year is constant. This has interesting implications for the choice of the fundamental space-time reference frames for positional astronomy. To explain 'precession', astronomers in the Ptolemaic tradition had assigned a slow but variable motion to the sphere of the fixed stars, a rotation about the pole of the ecliptic. (This was, of course, superimposed on the daily rotation, which was common to all the pre-Copernican theories.) The fixed point of zero celestial longitude was taken at one of the intersections of the great circle of the ecliptic with the extension of the Earth's equatorial plane; and time was measured by the Sun's passage through that point—the equinoctial year.

If, as Copernicus advocated in the *Commentariolis*, we change the definition of the standard year from equinoctal to sidereal (measured by the Sun's return to a given fixed star), an anomaly appears. For then it would be against an irregularly moving space frame (the sphere of fixed stars) that the motions defining uniform time would be measured. This contradicts all principles of harmony in the celestial motions, and such a system cannot serve as a fundamental space-time reference frame for astronomical science. Hence we need a different set of relative motions of the elements of the universe. (I should add here that the justness of the 'sidereal' measure of uniform motion was supported by other slowly varying parameters, or so appeared to Copernicus when he wrote the *Commentariolis*.)

One solution lies in a modification of a theory propounded by Copernicus's teacher, Domenicus Maria de Novara. This was that the Earth's equatorial plane is in motion; it was advanced to explain a supposed change of terrestrial latitudes (measured by the elevation of the pole) since antiquity. Giving the Earth's axis a slow conical motion (the 'Third Motion' of the mature Copernican theory) would free the stellar sphere of its trepidations, and give a harmonious reference-frame with 'sidereal' measures of space and time. It would also explain perfectly another fact reported by Copernicus in the *Commentariolis*: over the ages, a longer equinoctal year had coincided with a slower rate of precession.

But if Copernicus got this far, he then encountered a very serious problem: if this motion occurred, then the direction of the pole of rotation of the heavens, as seen by an observer, would have suffered an impossibly great change since antiquity. My conjecture rests on Copernicus getting this far with the problem, and then taking the only way out which would keep harmony in the heavens: letting the Earth rotate on its axis, while the axis performs the very slow conical motion. With this solution, the problem of the varying direction of the pole disappears. The principle behind the difference between the two solutions is that the finite rotations of a sphere do not commute.

My conjecture thus takes me to the first half of the 'Revolution'. Its extension to the annual revolution is something on which I have no ideas. Even this much bears on Copernicus's conviction of the truth of his theory, in spite of its physical, cosmological and theological difficulties. Sun and circle worship, and mathematical elegance, play their part, but a belief in the rationality and intelligibility of God's heavens may have been crucial.

There are two obvious objections to the principle of this conjecture. The first is that it requires Copernicus to have used two sets of false data (varying length of tropical year, and varying rate of precession), in such a fashion as to get consistent results, and without realizing their systematic connexion. This is easy to explain, for one and the same observational error (misreading the declination of the Sun, and hence misplacing the celestial equator) is responsible for both; orders of magnitude of observation error (5′), and errors of time and precession rate, work out correctly. There is also the fact that Copernicus made no mention of the precession problem in the *Commentariolis*, either in the text or in the introduction. This is not surprising, for at the time of writing it he had not worked out a precise mathematical theory of the 'Third Motion'. It is quite likely that Copernicus was able to work out the heliostatic equant-free planetary models with ease, using the geostatic equant-free models of Ibn Al-Shatir[4]. But on those problems which had engaged and persuaded him "in the first place", he would hold back his solutions until they could stand up to detailed criticism.

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[1] In Rosen, E., *Three Copernican Treatises*, second ed., 136 (New York: Dover, and London: Constable, 1959).

[2] Quoted from Kuhn, T., *The Copernican Revolution* (Cambridge: Harvard University Press, 1957), p. 138. Prof. Kuhn suggested there a possible connexion between calendar reform and the heliostatic hypothesis (p. 271), and he has given me generous and valuable assistance in connexion with this study.

[3] Rosen, *op. cit.*, 65.

[4] Kennedy, E. S., and Roberts, Victor, *Isis*, **50**, 227 (1953).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, March 13

INSTITUTION OF MECHANICAL ENGINEERS, INDUSTRIAL ADMINISTRATION AND ENGINEERING PRODUCTION GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 10 a.m.—Informal Discussion on "Human Capabilities and Limitations in Industrial Operations".

BRITISH SOCIETY FOR THE PHILOSOPHY OF SCIENCE (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. Karl Menger: "A Counterpart of Occam's Razor".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Town Planning and Electrical Requirements".

SOCIETY OF CHEMICAL INDUSTRY, AGRICULTURE GROUP (joint meeting with the SURFACE ACTIVITY GROUP, at 14 Belgrave Square, London, S.W.1), at 5.30 p.m.—Mr. G. H. Cashen: "Electric Charges on Clays".

UNIVERSITY OF LONDON (at King's College, Strand, London, W.C.2), at 5.30 p.m.—Prof. Marcel Simon (University of Strasbourg): "Origins and Eschatology".* (Further lecture on March 14.)

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Mr. C. E. Engel: "Photography in Medicine" (Cantor Lecture).

Tuesday, March 14

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

INSTITUTION OF THE RUBBER INDUSTRY, LONDON SECTION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 5.30 p.m.—"The Union of Rubbers and Plastics", speaker from Polymer (U.K.), Ltd., 7 p.m.—Mr. C. H. Leigh-Dugmore: "Light Microscopy of Black-Loaded Rubber"; Dr. E. H. Andrews: "Electron Microscopy of Black-Loaded Rubber".

UNIVERSITY OF LONDON (in the Gustave Tuck Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. G. D. Sims: "Thermionic Generation".* (Fourth of five lectures on "Generation of Electricity without the Use of Rotating Machinery".)

INSTITUTION OF ELECTRICAL ENGINEERS, EDUCATION DISCUSSION CIRCLE (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "New Routes into National Certificate and Technician Courses", opened by Mr. H. W. French.

Wednesday, March 15

ROYAL MICROSCOPICAL SOCIETY (at Tavistock House South, Tavistock Square, London, W.C.1), at 10.30 a.m.—Symposium on "Applications of Interference Microscopy".

ROYAL INSTITUTE OF CHEMISTRY (joint meeting with the INSTITUTE OF PHYSICS and the PHYSICAL SOCIETY and the INSTITUTE OF BIOLOGY, in the William Beveridge Hall, Senate House, University of London, W.C.1), at 2 p.m.—Symposium on "The Soil: Problems Raised by its Use and Misuse".

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Dr. S. Tolansky, F.R.S.: "The Folk Lore and History of Diamond".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 p.m.—Dr. W. L. Godson: "Total Ozone and the Middle Stratosphere Over Arctic and Sub-arctic Areas in Winter and Spring".

ROYAL SOCIETY OF MEDICINE, COMPARATIVE MEDICINE SECTION (at 1 Wimpole Street, London, W.1), at 5 p.m.—Meeting on "Hormonal Control of Fertility in Man and Animals".

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. A. J. Groszek and Mr. D. J. Palmer: "Surface-Active Compounds in Lubricating Oils".

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Magneto-Hydrodynamic Generation of Electricity" opened by Dr. P. L. Davies and Dr. D. J. Harris.

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (joint meeting with the GRADUATE AND STUDENTS SECTIONS of the INSTITUTIONS OF CIVIL AND MECHANICAL ENGINEERS, at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 6.30 p.m.—Prof. Sir Harrie Massey, F.R.S.: "Space Research".

SOCIETY OF INSTRUMENT TECHNOLOGY, DATA PROCESSING SECTION (at 26 Portland Place, London, W.1), at 7 p.m.—Symposium on "Burst Slug Detection in Nuclear Power Stations".

BRITISH PSYCHOLOGICAL SOCIETY, SOCIAL PSYCHOLOGY SECTION (in Room 425, Birkbeck College, Malet Street, London, W.C.1), at 8 p.m.—Mr. Joseph Trenaman: "Television and Political Images".

Thursday, March 16

INSTITUTE OF PHYSICS and the PHYSICAL SOCIETY, OPTICAL GROUP (at 47 Belgrave Square, London, S.W.1), at 2.30 p.m.—Annual General Meeting.

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.15 p.m.—Meeting for the Election of Fellows, 4.30 p.m.—Mr. F. P. Bretherton and Lord Rothschild, F.R.S.: "Rheotaxis of Spermatozoa"; Mr. D. J. Crisp and Mr. A. J. Southward: "Different Types of Cirral Activity of Barnacles with special reference to Sessile Species".

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. F. R. Keogh: "On a Problem of Hardy and Littlewood concerning Rearrangements".

BRITISH INSTITUTION OF RADIO ENGINEERS, ELECTRO-ACOUSTICS GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. S. Welldon: "Transistorized Tape Recorders".

INSTITUTION OF ELECTRICAL ENGINEERS, UTILIZATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. D. S. Farr, Mr. H. C. Hall and Dr. A. L. Williams: "A Dynamic Model for Studying the Behaviour of the Overhead Equipment used in Electric Railway Traction".

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. J. A. Reis, Miss Barbara E. Sabey and Mr. J. G. James: "White Line Road-markings and Light Coloured Road Surfaces".

ASSOCIATION OF CLINICAL BIOCHEMISTS (in the Lecture Theatre, Royal Free Hospital Medical School, Hunter Street, London, W.C.1), at 7.30 p.m.—Prof. H. B. Collier: "Recent Advances in Red Cell Chemistry".

CHEMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Prof. A. N. Terenin: "Charge Transfer in Organic Solids, Induced by Light" (Centenary Lecture).

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (at the Royal Army Medical College, Millbank, London, S.W.1), at 7.30 p.m. Laboratory Meeting. Chairman: Sir William MacArthur, K.C.B.

Friday, March 17

SOCIETY FOR WATER TREATMENT AND EXAMINATION (in the Library, Royal Society of Health, 90 Buckingham Palace Road, London, S.W.1), at 9.30 a.m.—Annual General Meeting, 10.30 a.m.—Symposium on "Application of Laboratory and Pilot Plant Studies to Full Scale Water and Effluent Treatment".

BRITISH PSYCHOLOGICAL SOCIETY, OCCUPATIONAL PSYCHOLOGY SECTION (in the Department of Psychology, Birkbeck College, Malet Street, London, W.C.1), at 1 p.m.—Mr. R. B. Buszard: "An Approach to the Classification of Working Environments".

INSTITUTE OF RURAL LIFE AT HOME AND OVERSEAS (at Friends International Centre, 32 Tavistock Square, London, W.C.1), at 1.15 p.m.—Mr. Peter du Sautoy: "The Ghana Community Development Programme".

INSTITUTE OF NAVIGATION (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—Captain V. A. M. Hunt: "The Long-Term Plan for Air Traffic Control".

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (joint meeting with the FINE CHEMICALS GROUP, at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. L. M. Jackman: "The Use of Nuclear Magnetic Resonance in the Determination of Chemical Structure".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. R. S. Nyholm, F.R.S.: "Magnetism and Chemical Architecture".

Saturday, March 18

NUTRITION SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 10.30 a.m. —Symposium on "The Place of Food Science and Technology in the Campaign against Malnutrition".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

BRITISH OIL AND CAKE MILLS RESEARCH FELLOW (graduate in agriculture, agricultural science or pure science, preferably with honours) IN THE DEPARTMENT OF AGRICULTURE—The Professor of Agriculture, The University, Leeds 2 (March 20).

SENIOR LECTURER IN METALLURGY—The Registrar, The University, Nottingham (March 24).

VICE-PRINCIPAL (with high academic qualifications and teaching experience at a high level)—The Clerk to the Governors, Chelsea College of Science and Technology, London, S.W.3 (March 24).

LECTURER IN APPLIED MATHEMATICS; a LECTURER or ASSISTANT LECTURER IN PURE MATHEMATICS; and a LECTURER or ASSISTANT LECTURER IN PURE or APPLIED MATHEMATICS—The Registrar, The University, Hull (March 29).

ASSISTANT CURATOR (with a university degree in biology and the Diploma of the Museums Association) IN NATURAL HISTORY at the St. Albans City Museum—The Town Clerk, 38 St. Peter's Street, St. Albans, Herts (March 31).

LECTURER or ASSISTANT LECTURER IN THE DEPARTMENT OF GENETICS—The Assistant Registrar (Science), The University, Edgbaston, Birmingham 15 (March 31).

RESEARCH FELLOW IN THE DEPARTMENT OF GEOLOGY—The Registrar, The University, Edgbaston, Birmingham 15 (March 31).

UNIVERSITY DEMONSTRATOR (with an honours degree in an appropriate science) IN AGRICULTURAL ENTOMOLOGY—The Secretary, School of Agriculture, The University, Downing Street, Cambridge (March 31).

HEAD (graduate, with research experience in such fields as genetics, avian physiology, nutrition or embryology, and preferably experience in any field of poultry science) OF THE POULTRY RESEARCH SECTION

The Secretary, Wye College (University of London), near Ashford, Kent (April 1).

Assistant Lecturer or Lecturer in Organic Chemistry at the University College of Rhodesia and Nyasaland—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 8).

Assistant Lecturer in Crop Production—The Secretary, Wye College (University of London), near Ashford, Kent (April 15).

Chair of Physics—The Registrar, The University, Sheffield (April 15).

Lecturer (honours graduate) in Physics—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (April 15).

Lecturer in Microbiology; and an Assistant Lecturer in Plant Ecology in the Department of Botany—The Secretary, University College, Gower Street, London, W.C.1 (April 15).

Lecturer (preferably with experience in techniques dealing with root infecting fungi) in Botany in the School of General Studies, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, April 15).

Lecturer or Assistant in Physiology—The Secretary of University Court, The University, Glasgow (April 29).

Research Professor in Nuclear Physics at the Victoria University of Wellington, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, May 1).

Assistant Trials Officers (preferably with practical experience in crop production) at Leeds University Farm, Headley Hall, Yorks., and at Seale-Hayne Agricultural College, Newton Abbot, Devon—The Secretary, National Institute of Agricultural Botany, Huntingdon Road, Cambridge.

Professors in Nuclear Physics, Physical Chemistry, and Hydraulic Engineering at the University of Peshawar—The Ministry of Labour (E.9), 26–28 King Street, London, S.W.1.

Senior Lecturer in Pharmacognosy; a Senior Lecturer in Pharmaceutics; a Senior Lecturer in Pharmacology; a Lecturer in Pharmaceutical Chemistry; a Lecturer in Pharmacognosy; a Lecturer in Pharmaceutics; and a Lecturer in Pharmacology—The Registrar (Department D), Bradford Institute of Technology, Bradford 7.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Privy Council. Medical Research Council Monitoring Report Series No. 1: Assay of Strontium-90 in Human Bone in the United Kingdom—Further Results for 1959. Pp. v + 18. (London: H.M. Stationery Office, 1960.) 1s. 6d. net. [212

Institute of Personnel Management. Occasional Papers, No. 16: Man and his Machines—Automation and Computation, their Origins and Effects. By Sir Ben Lockspeiser. Pp. 12. (London: Institute of Personnel Management, 1960.) 2s. 6d. [212

Department of Scientific and Industrial Research. Summary of Progress of the Geological Survey of Great Britain and the Museum of Practical Geology for the year 1959, with Report of the Geological Survey Board. Pp. iii + 76. (London: H.M. Stationery Office, 1960.) 5s. net. [212

Ministry of Housing and Local Government. River Severn Basin: Hydrological Survey (Hydrometric Area No. 54). Pp. iv + 135. (London: H.M. Stationery Office, 1960.) 17s. 6d. net. [212

Catalogue of Reproductions of Celestial Photographs published by the Royal Astronomical Society. Pp. 39. (London: Royal Astronomical Society, 1960.) [212

Report of the Woolfson Foundation, 1955–1960. Pp. 39 (8 plates). (London: The Woolfson Foundation, 1960.) [612

Technical Books-in-Print, Vol. 1, No. 8: Physics and Mathematics (September 1960). Edited by W. G. Smith, F.L.A. Pp. 60. (London: Hansom Books, Ltd., 1960.) 6d. [612

The British Council. Annual Report, 1959–60. Pp. vi + 110 + 12 plates. (London: The British Council, 1960.) [612

Titration in Non-Aqueous Solvents. By A. H. Beckett and E. H. Tinley. Third edition. Pp. iv + 56. (Poole: British Drug Houses, Ltd., 1960.) [612

Eton College Natural History Society. Fifteenth Report 1959–1960. Pp. 28 + 2 plates. (Eton: Eton College Natural History Society, 1960.) Non-members 2s. 6d.; Associates 1s. [612

The Manchester Joint Research Council. An Account of some of the Scientific and Technological Facilities which Manchester University and Manchester College of Science and Technology can offer to Industry. Pp. 19. Sources of Scientific and Technical Information available to Local Industry. Pp. 21. (Manchester: Manchester Joint Research Council, 1960.) [612

Southern Regional Council for Further Education. Thirteenth Annual Report, October 1960. Pp. 36. (Reading: Southern Regional Council for Further Education, 1960.) [612

Ministry of Health: Department of Health for Scotland. Radiological Hazards to Patients—Second Report of the Committee. Pp. ii + 114. (London: H.M. Stationery Office, 1960.) 6s. net. [612

Department of Scientific and Industrial Research. New Ways with Rubber. Pp. 16. (London: Department of Scientific and Industrial Research, 1960.) [612

National Physical Laboratory. Mathematical Tables, Vol. 4: Tables of Weber Parabolic Cylinder Functions and other Functions for Large Arguments. By L. Fox. Pp. iii + 40. (London: H.M. Stationery Office, 1960.) 12s. 6d. net. [1312

Building Research Station Digest, Second Series, No. 5: Materials for Concrete. Pp. 4. (London: H.M. Stationery Office, 1960.) 6d. [1312

Other Countries

Annual Report of the Calcutta School of Medicine and the Carmichael Hospital for Tropical Diseases, 1958–1959. Pp. 1 + 126. (Calcutta: Calcutta School of Tropical Medicine, 1960.) [212

Canada: Department of Mines and Technical Surveys. Publications of the Dominion Astrophysical Observatory, Victoria, B.C. Vol. 11, No. 9: The Spectroscopic Orbit of θ^2 Tauri. By E. G. Ebbighausen. Pp. 235–245. Vol. 11, No. 10: The Spectroscopic Orbit of γ Orionis. By E. G. Ebbighausen and R. M. Petrie. Pp. 247–252. Vol. 11, No. 11: Shock Waves in the Atmosphere of a Long-Period Variable. By G. J. Odgers and R. S. Kushwaha. Pp. 253–258. Vol. 11, No. 12: The Spectroscopic Binary H. D. 95638. By R. M. Petrie. Pp. 259–264. Vol. 11, No. 13: The Orbit of the Spectroscopic Binary ω Ursae Majoris. By E. G. Ebbighausen. Pp. 265–275. Vol. 11, No. 14: The Spectroscopic Orbit of β Trianguli. By E. G. Ebbighausen. Pp. 277–282. Vol. 11, No. 15: A Line Intensity Study of the Spectrum of H.D. 188001, 9 Sagittae. By Anne B. Underhill. Pp. 283–306. (Ottawa: Queen's Printer, 1960.) [212

Kodak Research Laboratories. Abridged Scientific Publications from the Kodak Research Laboratories, Vol. 35, 1953. Pp. ix + 135. (Rochester, N.Y.: Eastman Kodak Company, 1960.) [612

Académie Royale de Belgique. Classe des Sciences. Mémoires. Tome 32, Fascicule 1: Contribution à l'Étude des Échanges d'Ions Hydrogène au cours du Cycle de la Contraction Musculaire. Par Dr. A. Distèche. Pp. ii + 169. 200 francs. Tome 32, Fascicule 2: Lettres d'Adolf Baeyer à son ami Jean Servais Stas. Par J. Gillis. Pp. 45. 40 francs. Tome 32, Fascicule 3: Ricerche sul Contatto di Superficie Algebriche Lungo Curve. Par Dionisio Gallarati. Pp. 78. 60 francs. (Bruxelles: Académie Royale de Belgique, 1960.) [612

Occasional Papers of the California Academy of Sciences, No. 28, (November 1, 1960): A New Species of *Megomphix* from California. By Allyn G. Smith. Pp. 3. (San Francisco: California Academy of Sciences, 1960.) [612

Smithsonian Miscellaneous Collections. Vol. 140, No. 4: The Cephalic Nervous System of the Centipede *Arenophilus bipuncticeps* (Wood) (Chilopoda Geophilomorpha, Geophilidae). By Michael A. Lorenzo. Pp. iii + 43 + 5 plates. (Publication 4425.) Vol. 142, No. 1: Facts and Theories Concerning the Insect Head. By R. E. Snodgrass. Pp. 61. (Publication 4427.) (Washington, D.C.: Smithsonian Institution, 1960.) [612

Agricultural Research Service, United States Department of Agriculture, in co-operation with the Oklahoma Agricultural Experiment Station. Production Research Report No. 40: Investigations at the Great Plains Field Stations, Woodward, Okla., and Mandan, N. Dak. By L. F. Locke, H. V. Eck, R. A. Stewart and R. J. Haas. Pp. 33. (Washington, D.C.: Government Printing Office, 1960.) [612

Bulletin of the Bingham Oceanographic Collection. Vol. 17, Article 2: Plankton Studies. By Georgiana B. Deevey. Pp. 86. (New Haven, Conn.: Peabody Museum of Natural History, Yale University, 1960.) 3 dollars. [612

The South African Institute for Medical Research. Annual Report for the year 1959. Pp. 166. (Johannesburg: South African Institute for Medical Research, 1960.) [612

University of California Publications in Geological Sciences. Vol. 36, No. 7: A Marine Carnivore from the Challam Miocene Formation of Washington—Its Correlation with Neomarine Faunas. By R. A. Stirton. Pp. 345–368. (Berkeley and Los Angeles: University of California Press; London: Cambridge University Press, 1960.) 75 cents. [612

United States Department of the Interior: Geological Survey. Topographic Instructions of the United States Geological Survey. Kelsh Plotter Procedures: Instructions in the standard operating procedures for the Kelsh Plotter, including a description of equipment. (Book 3—Mapping Procedures. Part 3F—Stereocompilation Procedures. Chapter 3F5—Kelsh Plotter Procedures.) Pp. vii + 29. 35 cents. Planimetric Map Compilation with Trimetrogon Photographs: Instructions for preparing small-scale maps and charts from Trimetrogon Aerial Photographs. (Book 3—Mapping Procedures. Part 3G—Special Photogrammetric Procedures. Chapter 3G1—Planimetric Map Compilation with Trimetrogon Photographs.) Pp. vii + 28. 30 cents. (Washington, D.C.: Government Printing Office, 1960.) [612

Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture, Bruxelles. Comptes Rendus de Recherches. No. 26 (Novembre, 1960): Travaux du Comité pour l'Étude des Maladies et de l'Alimentation du Bétail (C.E.M.A.). Pp. 133. (Bruxelles: Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture, 1960.) 145 francs. [1312

Canada: Department of Northern Affairs and National Resources. National Museum of Canada. Bulletin No. 167: Contributions to Anthropology, 1958. Pp. v + 131 (15 plates). (Ottawa: Queen's Printer, 1960.) 2 dollars. [1312

National Science Foundation: Office of Science Information Service. NSF-60-65: Current Research and Development in Scientific Documentation, No. 7. Pp. viii + 153. (Washington, D.C.: Government Printing Office, 1960.) 65 cents. [1312

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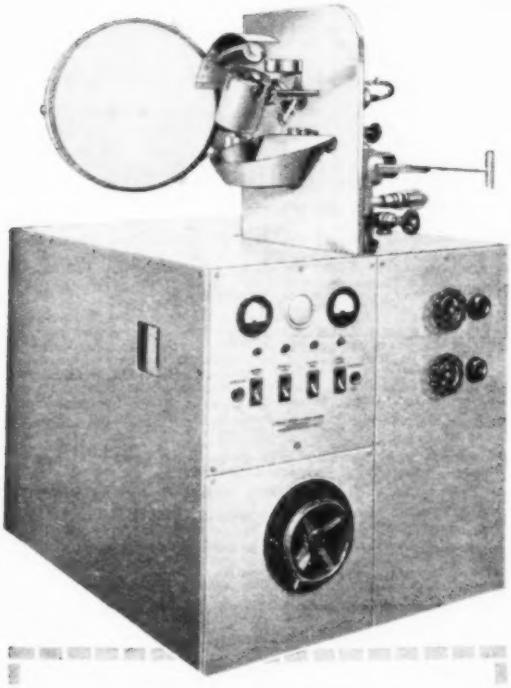

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APPOINTMENTS VACANT

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PRINCIPAL LECTURESHIPS
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The Department of Mechanical Engineering requires engineers and applied scientists to specialize in one or other of the following fields: Mechanical Vibrations; Control Systems either Hydraulic or Electro-Mechanical Mechanisms; Engineering Design; Applied Thermodynamics; Fluid Mechanics and in particular Aerodynamics; Strength of Materials; Aeronautical Structures; Welding Technology; Production Engineering Technology; Work Study; Engineering Management Studies.

These vacancies offer excellent opportunities for technologists to develop their knowledge and experience in one of those fields in a stimulating atmosphere in which personal initiative and individual responsibility are particularly welcomed and valued. This advertisement is directed towards persons with no teaching experience as well as to those with such experience. The present staff of the Department are helping to build up this College of Advanced Technology into a centre of advanced technological studies and research. Staff are expected to develop actively special knowledge in their particular spheres and to carry out research or other technological work as appropriate with postgraduate students or individually. They are also expected to foster the close relations already established with industry which are essential for future development; to this end, staff may engage in consulting work subject to reasonable safeguards. Laboratories, facilities and laboratory staff are excellent and are all currently being substantially increased.

Applicants should normally have an honours degree in engineering or an applied science, and, for the Lectureships and more senior posts, have had good research or industrial experience. Salaries are in the ranges: Principal Lecturers, £1,750 rising to £1,900 per annum; Senior Lecturers, £1,550 rising to £1,750 per annum; Lecturers, £1,370 rising to £1,550 per annum; Assistant Lecturers, £700 rising to £1,150 per annum. In each case, the starting salary will depend on qualifications and experience.

Further particulars and forms of application may be obtained from the Registrar, Royal Technical College, Salford 5, Lancs, to whom applications should be returned by April 1, 1961.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for Imperial Chemical Industries Fellowships tenable at the University College of North Staffordshire. Fellowships may be awarded for the purpose of carrying out original research in chemistry or physics, for a period not exceeding three years. Applicants should preferably hold the degree of Ph.D. or have equivalent research experience. Annual stipend will depend upon age, qualifications and experience, but will be within the range £800 to £1,100, together with F.S.S.U. benefits.

Applications (two copies), stating age, details of education, career and qualifications, publications and an outline of the proposed research, together with the names of two referees, should reach the Registrar, University College of North Staffordshire, Keele, Staffs, from whom further inquiries may be made, not later than March 31, 1961.

UNIVERSITY OF LONDON
KING'S COLLEGE

The College will require, on October 1, 1961, an Assistant Lecturer in Mathematics. Applicants should have a good Honours degree in Mathematics. An interest in Numerical Analysis will be welcome but not necessary.

Salary scale: £800 by £50 per annum to £950. A London allowance of £60, family allowances, and F.S.S.U. benefits will also be payable.

Full conditions of appointment and application forms may be obtained from the Registrar, King's College, London, Strand, W.C.2, completed forms must reach him by April 17.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH CHEMIST OR BIOCHEMIST
(No. 300/300)

The Organization's **Division of Food Preservation** invites applications for a senior position as Research Chemist or Biochemist in the Animal Products Section of the Division's new laboratories in Sydney, N.S.W. Applicants should be Honours graduates in Science or Agricultural Science with some years postgraduate research experience preferably in food science.

The research programme on animal products has hitherto been concerned with fish and eggs, but the work will now be expanded to include meat, meat products, and poultry. The appointee will be required to take a leading part in chemical and biochemical aspects of basic investigations in this field and will be given a considerable measure of freedom in choosing appropriate research projects.

Salary: Dependent on qualifications and experience within the ranges: £A 2,980 to £3,500 per annum, or £A 2,395 to £A 2,720 per annum.

Salary for a woman will be £A 160 per annum less than corresponding rates for men.

ENGINEERING PEDOLOGIST/GEOLOGIST
(No. 277/18)

The Organization's **Soil Mechanics Section, Melbourne, Victoria**, invites applications for appointment as Engineering Pedologist/Geologist from Honours graduates in Science or Engineering with Geology and/or Earth Science as a major subject and postgraduate research experience in pedology, sedimentary geology or geotechnology. Familiarity with collating and computing techniques an advantage.

The appointee will be required to analyse the fundamental and engineering significance of all measured and measurable physical and chemical properties of Australian soils; to assess in quantitative terms the validity of pedological and other soil classification systems in relation to engineering land use; and to develop, if necessary alternative systems for the appraisal and expression of basic soil properties. He would be expected to travel widely in Australia (and possibly overseas) to obtain first-hand experience of soil occurrences and properties and to study methods of classification and interpretation.

Salary: Dependent on qualifications and experience within the range: £A 1,510 to £A 2,265 per annum.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fare paid. Further information of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2.

to whom applications (quoting relevant Appointment number) should be addressed by April 15, 1961.

UNIVERSITY OF LEEDS
DEPARTMENT OF BIOCHEMISTRY

Applications are invited for appointment as Lecturer or Assistant Lecturer in Biochemistry. Salary scale for a Lecturer is £1,350 by £100 to £1,750 (efficiency bar) by £100 to £1,850 by £125 to £2,100 if medically qualified, or on the scale £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar at £1,550) if non-medically qualified, and for an Assistant Lecturer on the scale £1,050 by £50 to £1,150 if medically qualified, or on the scale £800 by £50 to £950 if non-medically qualified.

Applications (three copies), stating date of birth, qualifications and experience, together with the names of three referees, should reach the Registrar, the University, Leeds, 2 (from whom further particulars may be obtained) not later than April 4, 1961; candidates overseas may apply in the first instance by cable, naming three referees in the United Kingdom.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY
MANRESA ROAD, LONDON, S.W.3

The Governing Body invite applications for the post of Vice-principal of the College. Candidates should have high academic qualifications and teaching experience at a high level. The Vice-principal would be expected to take part in the administrative work of the College and should have had some experience in this field. Salary: £2,550 by £75 to £2,775 per annum, plus the appropriate London allowance.

Further particulars may be obtained from the Clerk to the Governors of the College by whom applications should be received not later than March 24, 1961.

VICTORIA UNIVERSITY OF WELLINGTON
NEW ZEALAND
RESEARCH PROFESSOR IN NUCLEAR PHYSICS

The Council of the Victoria University of Wellington proposes to appoint a Research Professor in Nuclear Physics within the Department of Physics and invites inquiries or applications from suitably qualified persons. An important function of the Research Professor will be to prosecute research work within the Institute of Nuclear Science which is situated in the Wellington area. The salary will be at the rate of £2,800 per annum. Approved fares to Wellington will be allowed for the appointee, his wife and his dependent children. In addition, actual removal expenses will be allowed within certain limits.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close in New Zealand and London on May 1, 1961.

UNIVERSITY OF BELFAST

The Senate of the Queen's University of Belfast invites applications for a Lectureship in Mechanical Engineering from October 1, 1961. Preference will be given to candidates who are interested in Strength of Materials. Salary range £1,050 to £1,850, plus contributory pension rights under the F.S.S.U. Initial placing on the salary scale will depend on qualifications and experience. Applications should be received by March 20, 1961.

Further particulars may be obtained from G. R. Cowie, M.A., LL.B., J.P., Secretary.

AUSTRALIA

THE UNIVERSITY OF NEW SOUTH WALES
FACULTY OF MEDICINE
TECHNICAL OFFICER
IN MACROSCOPIC PATHOLOGY

The University invites applications for appointment to the position of Technical Officer (Macroscopic Pathology) in the newly established School of Pathology, Kensington. Salary: £A.1,213 range £A.1,776 per annum. Commencing salary according to qualifications and experience. Applicants should possess a University degree and/or diploma in medical technology; previous experience in a workshop or a laboratory of pharmacology or immunology is desirable, though not essential. Duties will include the establishment of a laboratory of macroscopic pathology for the preparation of gross specimens for teaching and display, and collaboration with a medical illustrator and a photographer, under the general direction of the Professor of Pathology, in developing a pathological display hall, as well as carrying out general supervisory duties. The successful applicant will be expected to take up duties as soon as possible, and subject to satisfactory medical examination will be eligible to join the State Superannuation Scheme. Fares to Sydney will be paid for successful applicant and family.

Four (4) copies of applications, together with a recent photograph and the names of two referees, should be lodged with the Agent General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded to the Appointments Section, The University of New South Wales, Box 1, P.O., Kensington, N.S.W., by airmail to reach there before March 31, 1961.

UNIVERSITY OF MALAYA IN KUALA LUMPUR

LECTURESHIPS OR ASSISTANT LECTURESHIPS IN ENGINEERING

Applications are invited for appointment to one post of Lecturer and three posts of Assistant Lecturer in Engineering, depending on the qualifications and experience of the successful candidates; applicants must be University graduates in Engineering, and should hold recognized professional qualifications. Preference will be given to persons qualified in the following fields: (a) Thermodynamics; (b) Electrical Engineering; (c) Concrete Technology. The salary for a Lecturer is £1,148 by £49 to £1,442/£1,540 by £56 to £1,820 and for an Assistant Lecturer £1,001 by £49 to £1,099. In addition, a variable allowance is at present paid at 35 per cent of basic salary, subject to certain maxima, together with expatriation allowance at specified rates. First-class sea passages are provided for the appointee and his family, and housing assistance is available.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. The closing date for the receipt of applications in Malaya and London is March 27, 1961.

BRADFORD INSTITUTE OF TECHNOLOGY

DEPARTMENT OF PHARMACY

Head of Department: J. M. Rowson, Ph.D., M.Sc., F.P.S., F.L.S.

Applications are invited for the following posts: Senior Lecturer in Pharmacognosy, Senior Lecturer in Pharmaceutics, Senior Lecturer in Pharmacology, Lecturer in Pharmaceutical Chemistry, Lecturer in Pharmacognosy, Lecturer in Pharmaceutics, Lecturer in Pharmacology. Candidates should possess the qualifications and experience to teach their subject to honours degree standard. Adequate facilities for research are available. Salary scales: Senior Lecturer, £1,550 to £1,750 per annum, Lecturer, £1,370 to £1,550 per annum. Previous industrial or research experience at a suitable level will be taken into account in fixing the commencing salary.

Further particulars and forms of application may be obtained from the Registrar (Department E), Bradford Institute of Technology, Bradford, 7.

HENRY PATTEN,
Clerk to the Governors.

QUEEN MARY COLLEGE

(UNIVERSITY OF LONDON)

Applications are invited for the post of Assistant Lecturer in Physics, tenable from October 1, 1961. Salary £800 by £50 to £950, plus a London allowance of £60, F.S.S.U. participation and Family Allowance of £50 for each child.

Application forms, obtainable from the Registrar, Queen Mary College, Mile End Road, E.1, to be returned by March 25.

CHEMISTS AND PHYSICISTS

required by

BRITISH-AMERICAN TOBACCO COMPANY LIMITED

for its Research and Development Establishment (Southampton). These are first-class openings in expanding research groups for graduates with or without experience but with a definite urge for research.

Attractive conditions in a primarily non-industrial area, with easy access to the New Forest and the Solent. Written applications to Personnel Dept. (No. 5).

British-American Tobacco Co. Ltd.,
Westminster House, 7 Millbank, London, S.W.1.

IMPERIAL CHEMICAL INDUSTRIES LIMITED

DYESTUFFS DIVISION

invite applications for the appointment of

LIBRARIAN

at their works in

GRANGEMOUTH, SCOTLAND

The Works' Library is part of the Division Library Department and the successful applicant will be required to take charge of this small Library and develop the service it gives. Candidates should have experience in a Technical Library preferably in industry or be either a Chartered Librarian or a Science Graduate.

In the first instance training would be given at the Division's Headquarters in Blackley, Manchester.

Applications, giving full particulars, should be sent to Staff Department, Hexagon House, Blackley, Manchester 9.

NATIONAL CHEMICAL LABORATORY, D.S.I.R., Teddington, Middlesex, requires Scientific Officers, Senior Scientific Officers for work on following topics: Inorganic Chemistry. Study of semiconducting materials derived from rare earths; x-ray crystallography, thermodynamic measurements on inorganic substances; application of x-ray and electron diffraction techniques to study of mechanism of corrosion; solid state chemistry of transition metals and rare earth elements. Physical Chemistry. Fundamental study of metal/gas reactions; physical chemistry of electron exchanging polymers; determination of free energy data from measurements of chemical equilibria; reaction calorimetry. Electrochemistry. Electrochemistry of rare earth metals and less familiar elements; study of corrosion and electrochemistry of solutions up to 350 degrees Centigrade. Organic Chemistry. Synthesis of organometallic compounds. Qualifications: first- or second-class honours degree or equivalent in chemistry. Senior Scientific Officer at least three years' postgraduate experience required. Salary: Senior Scientific Officer, £1,392 to £1,714; Scientific Officer, £773 to £1,267.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting ref. F.105/1A. Closing date March 25, 1961.

NEUTRON PHYSICS

National Physical Laboratory, Teddington, Middx, requires officers to work in field of neutron physics. (1) In Scientific Officer class (Ref. A.72/1A), both Physicists and Chemists, to initiate and assist in neutron cross-section measurements, precision measurements of nuclear level schemes, and construction of semi-conductor detectors for nuclear radiations. Also in field of crystal diffraction as applied to neutron and gamma-ray spectroscopy. Qualifications: first- or second-class honours degree in physics or chemistry, or equivalent. Salary: Scientific Officer, £773 to £1,267; Senior Scientific Officer, £1,392 to £1,714 (at least three years postgraduate research experience required). (2) Experimental Officers (Ref. A.73/1A) to work with Scientific Officers on above duties. Qualifications: Pass degree, H.N.C. in applied physics or chemistry, or equivalent. Age not below 26. Salary: £1,132 to £1,386.

Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting appropriate reference.

UNIVERSITY OF THE WITWATERSRAND

JOHANNESBURG

LECTURER IN DEPARTMENT OF BOTANY

Applications are invited for appointment to the above post. Duties to be assumed on July 1, 1961, or as soon as possible thereafter. The salary will be according to the scale R.2,460 by R.120 to R.3,420 (£1,230 by £60 to £1,710). A commencing salary above the minimum notch may be paid on the grounds of special qualifications or experience. In addition, the University is at present authorized to pay an annual vacation savings bonus of up to R.120 in September each year. Membership of the University Institutions Provident Fund is compulsory, and membership of the University Staff Medical Aid Fund is compulsory in the case of an officer who is found eligible in terms of the rules.

Intending applicants are advised to obtain a copy of the Information Sheet relating to this vacancy from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in South Africa and London, on April 30, 1961.

UNIVERSITY OF EXETER

Applications are invited for two posts as Lecturer or Assistant Lecturer in the Department of Physics. Candidates with experience in upper atmosphere physics or in the physics of surfaces will be welcomed, though the appointments will not necessarily be restricted to these fields. Salary scales: Lecturer, £1,050 to £1,850 per annum (efficiency bar at £1,475); Assistant Lecturer, £800 to £950 per annum.

Applications, which should include the names of three referees, should be sent to the Secretary, The University, Exeter, from whom further particulars may be obtained. Closing date for applications (eight copies—overseas applicants one copy) April 10.

Pfizer invites

Pharmacologists Pharmacists
Physiologists Zoologists

to apply for graduate appointments at senior and junior levels in its Pharmacological Research Department. The work of the Department is divided between the examination of compounds synthesised in the Company's Chemical Research Department and basic research into the mode of action of drugs from the physiological, pharmacological, biochemical, and pathological points of view.

The Department has high standards and excellent facilities, and is a particularly happy working group. In general, conditions of work within the Company are very good, and staff have a choice of residence in coastal or inland East Kent towns.

Please send details of your experience and qualifications to the

PERSONNEL OFFICER (RESEARCH),
PFIZER LTD., SANDWICH, KENT

THE Pfizer GROUP
CHEMICALS · PHARMACEUTICALS · VACCINES
AGRICULTURAL & VETERINARY PRODUCTS

THE DISTILLERS COMPANY LIMITED

SHIFT SUPERVISOR

The Company wish to appoint a Shift Supervisor in the Pilot Plant Division of their Central Research Department at Tonbridge, Kent.

Candidates, aged not over 40, should hold a degree or equivalent qualification in Chemistry or Chemical Engineering. Production experience is not essential, although some knowledge of plant operation would be an advantage.

The post will involve responsibility for pilot plant operation on a shift basis, and the supervision of a team of process operators.

Quote Ref.: 13/61.N.

SHIFT TECHNICAL ASSISTANTS

The Company wish to appoint several Shift Technical Assistants in their Central Research Department at Epsom and at the Pilot Plant Division, Tonbridge, Kent.

Candidates, aged not over 40, should hold at least O.N.C. in Chemistry or an equivalent qualification. Previous experience is not essential, but some knowledge of analytical procedures would be an advantage. The posts will involve responsibility on a continuous shift basis for analytical control work, in connection with pilot plant operations. Shift technical assistants must be capable of critically appraising results so that techniques may be improved.

Quote Ref.: 14/61.N.

Write:
STAFF MANAGER
THE DISTILLERS COMPANY LIMITED
21/22 BOLTON STREET
LONDON, W.1.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

TAXONOMIC BOTANIST

(THREE YEAR APPOINTMENT)

The Organization's **Organic Chemistry Section of the Chemical Research Laboratories, Melbourne,** invites applications for the position of Taxonomic Botanist to work in the Territory of **Papua and New Guinea.** Applicants should be Honours graduates in Science or Agricultural Science, majoring in Botany (or hold equivalent qualifications) with postgraduate research experience, preferably in the field and herbarium. Experience in field collection an advantage.

The Section has for a number of years been studying the chemistry and pharmacology of plants from north-eastern Australia and is now extending the work to flora in Papua and New Guinea where the appointee will be based, initially at Lee. He will be responsible for the collection and identification of plant materials and will be expected to carry out critical floristic and taxonomic studies of the material, for which he will be given opportunity each year to spend time in Australian herbaria. He will spend extended periods in the field accompanied by a chemist to assist in carrying out chemical tests on materials collected.

Salary: Dependent on qualifications and experience within the ranges: £A.2,085 to £A.2,840 (married), £A.1,735 to £A.2,490 (single) per annum; or £A.2,995 to £A.3,320 (married), £A.2,620 to £A.2,945 (single) per annum.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit within which the original appointment is made.

Return fares paid. Further particulars and the special conditions applicable to this post will be supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 606/22) should be addressed by April 22, 1961.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF BOTANY AND PLANT TECHNOLOGY

Applications are invited for the following appointments in Mycology and Plant Pathology:

Lecturer to assist mainly in the teaching of a one year, full-time postgraduate course in Mycology and Plant Pathology. Salary scale £1,050 by £50 to £1,400 by £75 to £1,550 (bar) by £75 to £1,850 per annum, plus £60 per annum London allowance. Commencing salary in lower part of scale.

Demonstrator to assist in the teaching of Mycology and Plant Pathology to undergraduates. Salary £500 by £50 to £600 per annum.

Research Assistant to work on the degradation of cell walls of higher plants by plant pathogens. Good knowledge of plant biochemistry will be essential. Salary £700 by £50 to £800 per annum.

All posts subject to F.S.S.U. membership and with family allowances.

Application forms and further details may be obtained from Professor W. O. James, F.R.S., Imperial College of Science and Technology, London, S.W.7. The closing date for applications is April 30, 1961.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

Assistant Experimental Officer required in Chemical Microbiology Department for work on cheese flavour. Candidates should be familiar with elementary chemical techniques and should possess pass degree or equivalent, or if under 22 G.C.E. "A" level in two subjects. Starting salary within range £450 10s. (at 18) to £776 (at 26), in scale to £983; pension scheme; five-day week.

Apply to Secretary, N.I.R.D., Shinfield Reading. Quote ref. 61/9

ROYAL TECHNICAL COLLEGE
SALFORD

(College of Advanced Technology)

LECTURESHIPS IN METALLURGY

Applications are invited for two appointments from persons having an honours degree in Metallurgy, a good knowledge of physical metallurgy, and experience in research in industry, in a university, or in a College of Advanced Technology. The persons appointed will teach metallurgical subjects, and will be required and encouraged to carry out research and assist in the development of a strong metallurgical team in the College, for which good facilities are being provided.

The salary scale for a Lecturer is £1,370 rising to £1,550 per annum. The commencing salary may be above the minimum. Above this grade there are senior posts for which the successful candidates can be considered at a later date.

Further particulars and forms of application may be obtained from the Registrar, Royal Technical College, Salford 5, Lancs., to whom applications should be returned by April 17th, 1961.

GLASS TECHNICIAN

A vacancy has arisen for an experienced man to work on experimental and production problems involving bench and mechanically-aided work. Must have experience of Glass and Metal Seals and previous work in Precision Glassware would be an advantage. This is a staff position, 38½ hour five-day week. Initial training on certain aspects of the work will be carried out in conjunction with the Hirst Research Centre at Wembley.

Please apply in writing, giving details of previous experience to:

Personnel Officer G/T,
M.O. Valve Co. Ltd.,
Brook Green, Hammersmith, W.6.

ROYAL TECHNICAL COLLEGE
SALFORD
DEPARTMENT OF ELECTRICAL ENGINEERING

Continued expansion of this College of Advanced Technology results in a limited number of vacancies for academic staff at all levels; salaries range from £700 to £2,100 per annum, or possibly higher in special cases. Applicants should be graduate electrical engineers or physicists. Considerable importance will be attached to proven ability in research, and commencing salaries will take account of past achievement. Lecturing hours, and equipment available, are such that a genuine opportunity exists for original work. Some posts may be primarily research appointments.

Further particulars and forms of application may be obtained from the Registrar, Royal Technical College, Salford 5, Lancs (please quote ref. N.), to whom applications should be returned by April 14, 1961.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Assistant Lecturer or Lecturer in the Department of Oceanography. Candidates should have an honours degree in Physical Oceanography or Physics, and should be prepared to spend several weeks each year at sea. The initial salary will be within the range £800 to £1,350 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than April 4, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Quoting reference CV/N.

SHELL

"SHELL" RESEARCH LIMITED

require

LABORATORY ASSISTANTS

in their Organic Synthesis Division at

WOODSTOCK AGRICULTURAL RESEARCH CENTRE

near Sittingbourne, Kent

Candidates should possess a good range of subjects at G.C.E. "O" Level, plus "A" Level in Chemistry, or H.N.C. or Part I Grad.R.I.C. Work will be connected with the discovery and development of new insecticides and herbicides. Upper age limit 35 years.

Five-day week, staff restaurant, attractive pension scheme, bus service to door.

Applications in writing to:

The Personnel Superintendent,
"Shell" Research Ltd.,
Woodstock Agricultural Research Centre,
Sittingbourne, Kent.

Pathologist

Pfizer Ltd. wishes to appoint a Pathologist in its Pharmacological Research Department at Sandwich in Kent. The person appointed will be concerned with research into the pathology of a variety of non-infectious diseases and infections in laboratory animals, and with the pathological evaluation of drug action during and after toxicological trials. In addition, the Pathologist will be engouraged to conduct research into subjects of his own choosing.

Applicants should have medical or veterinary qualifications; experience of histo-chemical techniques will be an asset.

Working conditions and terms of employment at Pfizer are very good, and staff have a choice of residence in coastal and inland East Kent towns.

Please send full details of yourself to the

PERSONNEL OFFICER (RESEARCH),
PFIZER, LTD., SANDWICH, KENT.

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CHEMICALS · PHARMACEUTICALS · VACCINES
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ARTHUR D. LITTLE RESEARCH INSTITUTE

PHYSICO CHEMICAL DIVISION

A DIVISION HEAD is required to direct basic studies into the bulk properties of polymers and to initiate research in his own field of interest.

Only physical chemists with outstanding qualifications and experience, and an original outlook should apply.

The initial salary offered is attractive and commensurate with qualifications and experience and there is an excellent Life Assurance and Pension Scheme in operation.

The Arthur D. Little Research Institute is a unique and expanding independent research organization offering great scope for scientists with original ideas in fundamental research and encouragement to publish results.

Applications giving full details of experience to the **Director, Arthur D. Little Research Institute, Inveresk, Musselburgh, Midlothian.**

United Kingdom Atomic Energy Authority and National Institute for Research in Nuclear Science

INSTRUMENTATION AND DATA HANDLING

for

NUCLEAR PHYSICS RESEARCH AT HARWELL

Scientists are required by the U.K.A.E.A. and by the National Institute for Research in Nuclear Science for the study of advanced instrumentation problems associated with the use of large particle-accelerators in Nuclear Research at the Atomic Energy Research Establishment and the Rutherford Laboratory, Harwell. They will collaborate closely with scientists conducting experiments with such machines as the Cyclotron, the Tanden van de Graaff, the Proton Linear Accelerator, the Neutron Booster and the 7 GeV. Accelerator now under construction. There is a wide variety of problems to be tackled, such as the use of scintillating materials or semi-conductors to record rare nuclear disintegrations or the paths of nuclear particles, high-speed information storage and specialised data handling for the analysis of nuclear events, and the measurement of time intervals of the order of 1 millimicro-second.

Preference will be given to candidates with experience in some of the above fields or in experimental Nuclear Physics, but all applicants should possess first or good second class honours degree, preferably in Physics or Electrical Engineering.

Salary will be according to experience in the following ranges.

Principal Scientific Officer:	**£1,840–£2,590 per annum**
Senior Scientific Officer:	**£1,440–£1,770 per annum**
Scientific Officer:	**£790–£1,310 per annum**

★ For three years postgraduate experience starting salary will be at least £1,010 per annum. Housing and contributory pension schemes.

Send POSTCARD for details to Personnel Manager (1888/34) U.K.A.E.A., A.E.R.E., Harwell, Didcot, Berks

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

ORGANIC CHEMIST

The Organization's **Division of Coal Research, Sydney, N.S.W.,** invites applications for a position as Organic Chemist from Graduates or holders of Technical College Diploma majoring in Organic Chemistry. Experience of distillation and chromatographic techniques an advantage.

The appointee will be required to assist on investigations of the chemical constitution of coal tar and pitch and in the development of new industrial uses for these materials. Opportunities available for acquiring experience in infra-red and U.V. spectroscopy, polarography and other techniques.

Salary: Dependent on qualifications and experience within the ranges: £A.1,620 to £A.1,950 per annum, or £A.2,070 to £A.2,330 per annum.

Salary for a woman will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further information of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 480/359) should be addressed by April 22, 1961.

PAINT RESEARCH STATION
ORGANO-METALLIC COMPOUNDS

Chemists are invited to apply for a post in a special project to study the role of organo-metallic compounds in paint. The work, mostly fundamental in character, will include both organic and physico-chemical studies. Applicants should have a good honours degree; a Ph.D. or equivalent research experience is desirable. Salaries will be commensurate with age and experience, with F.S.S.U. superannuation.

Applications, giving full details of qualifications and experience, and the names of two references, should be made in writing to the Director, The Research Association of British Paint, Colour and Varnish Manufacturers' Paint Research Station, Waldegrave Road, Teddington, Middlesex.

INSTITUTE OF CHILD HEALTH
(UNIVERSITY OF LONDON)

Applications are invited for the post of Senior Technician (Whitley Scales) to assist in work on lung function. Applicants should have had experience in a physiological laboratory.

Apply to the Secretary, Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, W.C.1.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Junior Technical Assistant required at Chester Beatty Research Institute, Fulham Road, S.W.3, for radiobiological studies. Ordinary or advanced level G.C.E. desired. Salary on M.R.C. scales, according to qualifications.—Apply with names of two referees to the Secretary, 33 Sumner Place, S.W.7, quoting ref. 301/B/54.

SENIOR SCIENTIFIC OFFICER/ SCIENTIFIC OFFICER

Applications invited for pensionable posts in the Crop and Animal Husbandry Division of the Ministry of Agriculture, Northern Ireland. Qualifications: Degree in agriculture with postgraduate experience in research and a sound practical knowledge of crop and animal husbandry. For Senior Scientific Officer post some years relevant postgraduate experience essential. For Scientific Officer post preference will be given to candidates with experience in pig husbandry research. Salary scales (under review): Senior Scientific Officer, £1,342 to £1,654; Scientific Officer, £738 to £1,222. A candidate with special qualifications, training or experience may enter scale above minimum. In addition to research work, teaching duties may have to be undertaken in the Faculty of Agriculture, Queen's University, Belfast. Preference for ex-Service candidates.

Application forms obtainable from Secretary, Civil Service Commission, Stormont, Belfast, and must be returned by March 29, 1961.

UNITED KINGDOM TECHNICAL ASSISTANCE

Professors in Nuclear Physics, Physical Chemistry and Hydraulic Engineering are required at the University of Peshawar, Pakistan, for two years. Salary: £2,680 to £3,600 per annum, according to qualifications and experience. Tax-free allowance—£1,680 per annum (married) £960 (single). Free furnished accommodation or refund of 45 per cent of basic hotel bills. Emoluments paid by U.K. Government.

Write to Ministry of Labour (E.9), 26/28 King Street, London, S.W.1, for further information.

NATIONAL CHEMICAL LABORATORY, D.S.I.R., Teddington, Middlesex, requires Assistant Experimental Officers/Experimental Officers for work on general inorganic chemistry, micro-analysis, electrochemistry, chemical thermodynamics, corrosion. Minimum qualifications—G.C.E. "A" level in chemistry and another science or mathematics subject or equivalent, but over 22 pass degree, H.N.C. in chemistry, or equivalent, expected. Salary: Assistant Experimental Officer, £478 (age 18) to £841 (age 26) to £1,023; Experimental Officer, £1,132 to £1,386.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting ref. F.106/1A. Closing date March 25, 1961.

ANIMAL HEALTH TRUST

WELLCOME VETERINARY RESEARCH FELLOWSHIPS

1961

Applications are invited for appointments to Wellcome Fellowships for whole-time research in connection with veterinary science or medicine, from any person who on October 1, 1961, is under 36 years of age and holds the Membership Diploma of the Royal College of Veterinary Surgeons or a good degree in any faculty relevant to veterinary science or medicine in any university in the British Commonwealth and Empire. Applicants are expected to have done some postgraduate work and to provide evidence that they have been able to make arrangements for the satisfactory conduct of the proposed research which must be in the broad field of veterinary science. A Fellowsip may be awarded at an annual value of £850 rising by annual increments of £50. The Fellowship is subject to income tax and carries benefits under the F.S.S.U.; it is tenable for one year in the first instance, and by annual reappointment for a further period of two years at the discretion of the Advisory Committee. Election will be made in June, to take effect as from October 1, 1961. Closing date for receipt of application is Friday, May 12, 1961.

Forms of application are obtainable from: The Scientific Director, The Animal Health Trust, 14 Ashley Place, Westminster, London, S.W.1.

BEECHAMS FOODS LIMITED

MICROBIOLOGY RESEARCH

A vacancy exists for a qualified assistant for interesting research work on all microbiological aspects of fruit juice and soft drinks processing at our laboratories in West Gloucestershire.

Applications are invited from men and women under 35 years who possess a General Degree in Microbiology or equivalent. Salary appropriate to qualifications and experience.

The Company operate non-contributory pension and profit participation schemes.

Applications should be addressed to Personnel Manager, Ref. M/R, Beecham House, Brentford, Middx.

UNIVERSITY OF QUEENSLAND

LECTURER IN BACTERIOLOGY

Applications are invited for the above-mentioned position. Applicants should have an honours degree in bacteriology, and preferably a higher degree, and some experience of research. Other things being equal, preference will be given to an applicant willing to undertake research in systematic bacteriology. Salary range £A.1,830 by £A.70 to £A.2,330. The successful applicant will enjoy the privileges of superannuation, study leave, travel grants, and other benefits available to the academic staff.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on April 15, 1961.

UNIVERSITY OF EXETER

Applications are invited for two posts of Lecturer or Assistant Lecturer in Chemistry; for one post, applicants should have special interests in organic chemistry and for the other, in physical or physical inorganic chemistry. Salary scales: Lecturers, £1,050 to £1,850 per annum (efficiency bar at £1,475); Assistant Lecturers, £800 to £950 per annum.

Further particulars may be obtained from the Secretary of the University, to whom applications (eight copies—overseas applicants one copy) giving the names of three referees, should be sent by April 17, 1961.

NORTHERN POLYTECHNIC

HOLLOWAY, LONDON, N.7

The Governing Body invites immediate applications for appointment as full-time Lecturer in Physics. The Department is concerned largely with university and advanced technological work and has substantial research in progress. Salary scale: £1,370 by £35 to £1,510 by £40 to £1,550, plus London allowance.

Apply for form of application and further particulars to the Clerk to the Governors.

WYE COLLEGE

(UNIVERSITY OF LONDON)

Applications are invited for the post of Head of the Poultry Research Section from graduates with research experience in such fields as Genetics, Avian Physiology, Nutrition or Embryology. Experience in any field of Poultry Science would be an advantage but is not necessarily considered to be essential. Associated with the Section is a small postgraduate school in Poultry Science and excellent research facilities are available. The appointment will be made in the Lecturer grade (£1,050 to £1,850) or Senior Lecturer grade (rising to £2,175), according to qualifications and experience.

Further particulars may be obtained from the Secretary, Wye College, near Ashford, Kent, to whom applications should be submitted by April 1, 1961.

UNIVERSITY OF GLASGOW

LECTURESHIPS IN EXPERIMENTAL AND THEORETICAL PHYSICS

Applications are invited for Lectureships in Experimental and Theoretical Physics. Salary scale: Senior Lecturer, £1,750 to £2,275 per annum; Lecturer, £1,050 to £1,850 per annum. Grade of appointment and initial salary according to experience and qualifications. F.S.S.U. and family allowance benefits. Successful applicants will be expected to prosecute research preferably in Nuclear or Elementary Particle Physics in addition to teaching duties.

Applications (eight copies), including the names of two referees, should be lodged, not later than April 15, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court.

UNIVERSITY OF MANCHESTER

Applications are invited for two posts of Lecturer in Engineering (Civil). The Department is to be rehoused in new buildings during the next academic year, and there are wide opportunities for research in all branches of Civil Engineering, including Hydraulics, Soil Mechanics, Reinforced Concrete and Metal Structures. The salary scale is £1,050 to £1,850 per annum; initial salary according to qualifications and experience. Membership of F.S.S.U. and Children's Allowance Scheme.

Applications should be sent not later than March 31, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained. Overseas applicants should send letters of application in the first instance, giving full details of qualifications and experience, and should submit the names and addresses of at least three persons to whom reference may be made.

AUSTRALIAN NATIONAL UNIVERSITY

SCHOOL OF GENERAL STUDIES
LECTURER IN BOTANY

Applications are invited for appointment to the post of Lecturer in Botany. The appointee will be required to conduct courses in mycology, and experience in techniques dealing with root infecting fungi will be an advantage. The salary range for a Lecturer is £A.1,640 by £A.90 to £A.2,360. Commencing salary will be in accordance with qualifications and experience.

Further information and the summary forms which must accompany an application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on April 15, 1961.

UNIVERSITY OF BRITISH COLUMBIA

PHYSICS

Applications are invited for appointments to the teaching and research staff as well as for postgraduate fellowships and scholarships for the Session commencing in September, 1961. There are specific vacancies at the Assistant Professor level in Optical Spectroscopy, Meteorology and Low Energy Theoretical Nuclear Physics. Applications in other fields of physics will also be considered.

Further information and a copy of an illustrated brochure describing the activities and facilities of the Department may be obtained by writing to G. M. Shrum, Head, Department of Physics, University of British Columbia, Vancouver 8, B.C. Professor Shrum expects to be in London from March 16 to 25 and will be pleased to arrange personal interviews. Inquiries should be directed to B.C. House, 1 Lower Regent Street, London, S.W.1.

UNITED KINGDOM TECHNICAL ASSISTANCE

Biochemist required by the Government of the Philippines for one to two years to advise and teach in the field of nutritional chemistry. Salary: £2,000 to £2,600 per annum, according to qualifications and experience. Tax free allowance of £2,260 (married) or £1,610 (single). Free furnished accommodation or allowance in lieu. All emoluments paid by the United Kingdom Government.

Write to Ministry of Labour (E9), 26 King Street, London, S.W.1, quoting, PHI/892.

THE PATENT OFFICE

OFFERS SCIENTISTS A CAREER WITH AN ASSURED FUTURE

SALARY. Starting salary within the scale £793 to £1,719 according to experience, with advances in the scale to £941 after two years and to £1,324 after 3 to 5 years, for those starting below these points. One promotion only (prospects excellent) raises maximum to £2,715. Further prospects up to £4,415.

QUALIFICATIONS. Age 21 to 36 and Degree or Diploma of Technology with first- or second-class honours in physics, chemistry, engineering or mathematics, or equivalent professional qualification, e.g., A.Inst.P., A.R.I.C., or corporate membership of I.C.E., I.Mech.E. or I.E.E.

INTEREST. The examination of patent specifications will maintain your knowledge of science and technology completely up-to-date and will give you inside knowledge of new manufactures well ahead of the public at large.

CONDITIONS. Location, London. Five-day week. Annual leave 4½ rising to 6 weeks with considerable freedom as to when it is utilized. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information or for a visit to see the work. *The Superintending Examiner (B. Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Holborn 8721, Ext. 324.*

UNIVERSITY OF ADELAIDE

WAITE AGRICULTURAL RESEARCH INSTITUTE

The University invites applications for appointment in the Department of Agronomy at the Waite Institute as Lecturer in Cytogenetics. Duties: To undertake cytogenetic studies as part of a cereal breeding and genetic research programme. Salary scale: £A.1,675 by £A.95 to £A.2,340, with superannuation on the F.S.S.U. basis. The Waite Institute has excellent field, glasshouse and laboratory facilities, including good optical equipment for cytological work. General conditions of appointment and a statement about the post may be had on application to the Registrar or to the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Any further information desired will gladly be supplied on application to the Registrar.

Applications, in duplicate, and giving the information listed in the final paragraph of the general conditions of appointment, should reach the Registrar, The University of Adelaide, Adelaide, South Australia, not later than April 17, 1961.

ONTARIO VETERINARY COLLEGE

GUELPH, ONTARIO, CANADA

Applications are invited for an appointment as an Assistant or Associate Professor in Pharmacology. Applicants should have a Ph.D. and teaching experience. The candidate will lecture to undergraduate and postgraduate students in pharmacology and be expected to undertake research in some aspect of the field.

A curriculum vitae and references should be addressed to Dr. H. G. Downie, Professor and Head, Department of Physiological Sciences.

OLDCHURCH HOSPITAL ROMFORD, ESSEX

(709 Beds)

RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

Assistant Experimental Officer required in physics department to assist in studies of physical properties of dairy products—butter and cheese, etc. He will also be required to construct and modify experimental testing equipment in the department workshop, and skill in using a lathe would be advantageous. Candidates should possess H.N.C. or pass degree, or if under 22 G.C.E. "A" level or equivalent. Starting salary within range £450 10s. (at 18) to £776 (at 26) in scale to £983; pension scheme.

Apply, naming two referees to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/4.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND

ST. JOHN'S, NEWFOUNDLAND, CANADA

Applications are invited for the position Assistant Professor of Biology with specialization in animal physiology, embryology and histology. Candidates with background and experience in marine biology will receive preference. Ph.D. or equivalent essential. Duties beginning September, 1961, to include teaching and research. The starting salary will be based on qualifications and experience.

Applications, accompanied by complete curriculum vitae and the names of three references, should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

UNIVERSITY OF ALBERTA

DEPARTMENT OF CHEMISTRY

TEACHING ASSISTANTSHIPS

$2,200 to $2,700 for eight months are open to qualified students proceeding to advanced degrees. Nine hours per week of laboratory instruction required. Active research programmes in analytical, inorganic, organic, physical and theoretical chemistry. Travel allowance.

Apply to: Professor Harry E. Gunning, Head Department of Chemistry, University of Alberta Edmonton, Alberta, Canada.

UNIVERSITY OF NEW ENGLAND

ARMIDALE, NEW SOUTH WALES

LECTURER IN PHYSICS

Applications are invited for a Lectureship in the Department of Physics. Commencing salary will be determined in accordance with qualifications and experience within the range £A.1,730 by £A.105 to £A.2,435 per annum, plus a cost of living adjustment which is at the moment £A.36 per annum. Superannuation and assistance in the buying or building of a house will be provided for a permanent appointee.

Further particulars about the position and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on April 30, 1961.

UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND

Applications are invited for (A) Assistant Lectureship or (B) Lectureship in Organic Chemistry. Salary scales: (A) £1,200 by £50 to £1,350 per annum. (B) Grade II, £1,350 by £50 to £1,600 per annum, Grade I, £1,600 by £50 to £1,900 per annum. Passages to Salisbury for appointee, wife and dependent children on appointment, with allowance for transport of effects. Superannuation and Medical Aid Schemes. Unfurnished accommodation at rent of 15 per cent of salary. Assistance given for triennial visits overseas.

Detailed applications (6 copies), naming three referees, by April 8, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF GLASGOW

LECTURESHIP OR ASSISTANTSHIP IN PHYSIOLOGY

Applications are invited for a Lectureship or an Assistantship in Physiology. Salary scale: With a medical qualification, £1,050 to £1,900 per annum for Lecturers, and £1,050 to £1,250 per annum for Assistants; without a medical qualification, £1,050 to £1,850 per annum for Lecturers, and £800 to £950 per annum for Assistants. Initial salary according to experience and qualifications. F.S.S.U. and family allowance benefits.

Applications (eight copies for the Lectureship, three copies for the Assistantship) should be lodged, not later than April 29, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for the post of Lecturer or Assistant Lecturer in Mathematics. Applicants should be qualified in Pure or Applied Mathematics. The appointment will start from October 1, 1961. Salary in scale £1,050 by £50 to £1,400 by £75 to £1,850 (Lecturers), £800 by £50 to £950 per annum (Assistant Lecturers), with F.S.S.U. and children's allowances.

Applications should reach the Registrar, the College, Keele, Staffs, from whom further particulars and application forms may be obtained, not later than March 25, 1961.

STOKE MANDEVILLE HOSPITAL

AYLESBURY

Assistant Biochemist required in the Area Pathology Laboratory based at the above Hospital. Applicants should possess first- or second-class honours degree in chemistry or biochemistry, or A.R.I.C. Whitley Council conditions of service. Salary £925 to £1,150 per annum after (for new entrants only) a probationary period. The post offers a wide variety of experience in a well-equipped and pleasant laboratory.

Applications, giving full details of qualifications, etc., together with names of two referees, to be forwarded to the Administrative Officer as soon as possible.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Assistant Lecturer in Biophysics in the Faculty of Medicine. The post is newly established and applicants should have been trained in electron microscopic techniques. Duties to commence June 1, 1961, or as soon as possible thereafter. Salary on a scale £800 to £950 per annum with membership of F.S.S.U. and Children's Allowance Scheme.

Applications should be sent not later than March 25, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

INSTITUTE OF CHILD HEALTH

UNIVERSITY OF LONDON

Laboratory Technician required for the Neonatal Unit at the Hammersmith Hospital, Ducane Road, W.12. Biochemical experience an advantage. A.I.M.L.T. or equivalent preferred. Salary, Senior Technician II, Whitley Scales.

Apply to the Secretary, Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, W.C.1, giving age, experience, and qualifications.

PERSONAL ASSISTANT/SECRETARY required for Head of Physiology Department, National Institute for Research in Dairying. Good secretarial qualifications and some relevant experience, or knowledge of biological science essential. A university degree (preferably in biological science) or equivalent desirable. Commencing salary according to age in scale £469 (age 21) to £568 (age 25 or over on entry) to £796 or for degree in biological science or equivalent, £578 (age 21) to £776 (age 26 or over on entry) to £983, with superannuation in each case.—Applications, naming two referees, to Secretary, N.I.R.D., Shinfield, Reading. Quote reference 61/10.

NUCLEAR CHEMISTRY GRADUATE APpointments open beginning July or September 1961, at stipends from $1,920 to $2,520 for fundamental work toward M.S. or Ph.D. degree. Twelve-month appointment with one month vacation. Excellent equipment for research on neutron induced nuclear reactions and decay schemes of radioactive nuclei using 400 KV. Cockcroft-Walton ion accelerator.—Write: Department of Chemistry, University of Arkansas, Fayetteville, Ark., U.S.A.

CITY OF LEICESTER EDUCATION COMMITTEE

LEICESTER COLLEGE OF TECHNOLOGY AND COMMERCE

Principal: R. E. Wood, M.Sc., F.Inst.P.

Applications are invited for the post of Senior Laboratory Technician in the Department of Biology. It is essential that applicants should have had experience in the treatment of animals under Home Office regulations, and in the organization of laboratories for biological subjects, including Pharmacology. The possession of an appropriate qualification is desirable. Salary is in accordance with Misc. Grade VI, £760 by £25 (1) by £20 (2) to £825.

Applications, giving full details, should be forwarded to the Registrar at the College.

UNIVERSITY OF LIVERPOOL

SUB-DEPARMENT OF NUMERICAL ANALYSIS

Applications are invited for the post of Computer Officer. The initial salary will be within the range £650 to £1,250 per annum, according to age, qualifications and experience.

Applications, stating age, qualifications and experience, together with the names of two referees, should be received not later than April 29, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Quoting Reference Number CV/N.

UNIVERSITY OF NOTTINGHAM

DEPARTMENT OF METALLURGY

Applications are invited for the appointment of Senior Lecturer in Metallurgy. Salary within the scale £1,850 by £75 to £2,225 per annum, according to qualifications and experience, with membership of the Universities' Superannuation System and children's allowance.

Conditions of appointment and form of application, to be returned by Friday, March 24, 1961, from the Registrar.

UNIVERSITY OF NOTTINGHAM

Applications are invited for the appointment of an Assistant Lecturer in Sociology. Salary scale £800 by £50 to £950 per annum, with membership of the Universities' Superannuation Scheme and children's allowance. Applications will be considered from candiates who expect to graduate in Sociology this year.

Conditions of appointment and form of application, to be returned by March 18, from the Registrar.

UNIVERSITY OF OTTAWA

DEPARTMENT OF CHEMISTRY

Applications are invited for an Associate Professorship in the field of organic chemistry. Candidates should be active research workers with several years' experience of University lecturing.

Applications, including a curriculum vitae, a list of published papers, and the names of two referees, should be sent as soon as possible to Professor K. J. Laidler, Department of Chemistry, University of Ottawa, Ottawa 2, Canada.

UNITED KINGDOM TECHNICAL ASSISTANCE

Agronomist/Agricultural Engineer required for the Rubber Research Institute of Ceylon for two years. To carry out experiments on the testing of spraying and dusting equipment. Also research on influence of coverage and particle size. Salary £2,500 per annum (subject to U.K. income tax), plus tax-free allowance £1,175 (married), £675 (single). Free furnished accommodation. All emoluments paid by the U.K. Government.

Apply to Ministry of Labour (E.9), 26 King Street, London, S.W.1, quoting CEY/42.

TECHNICAL SALES REPRESENTATIVE required by City firm dealing in Industrial Chemicals and raw materials for the electronic industry. University degree and some knowledge of French essential. Salary according to age and qualifications, within the £750 to £1,500 range. Superannuation Scheme. Age preferably 25 to 30.—Box 954, T. G. Scott & Son, Ltd., 1 Clement's Inn, London, W.C.2.

GRADUATE CHEMIST OR PHYSICAL Chemist (age 23-30 years) is required for work on techniques employed in the fractionation of proteins in human plasma. This work includes the development of laboratory procedures for use on a small production scale. This post provides a unique opportunity of gaining experience in physico-chemical methods of separating proteins.—Apply in writing, stating age, qualifications and experience, and with names of two referees, to Secretary, Lister Institute of Preventive Medicine, Elstree, Herts.

PULP AND PAPER RESEARCH INSTITUTE OF CANADA
MONTREAL

requires

FLUID DYNAMICIST

To conduct theoretical and experimental studies on the various aspects of the paper-making process including turbulent phenomena in fibre suspensions, dynamics of drainage, sheet formation, sheet pressing, drying, etc.

Qualifications: Ph.D. or equivalent in research experience in hydro- or aero-dynamics. Experience in papermaking field not essential.

Apply, enclosing comprehensive job résumé, to:

Chief Personnel Officer,
Pulp and Paper Research Institute of Canada,
3420 University Street,
Montreal, Quebec.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND
ST. JOHN'S, NEWFOUNDLAND, CANADA

Applications are invited for the position Assistant Professor of Biology with specialization in invertebrate zoology. Candidates with background and experience in marine biology will receive preference. Ph.D. or equivalent essential. Duties beginning September, 1961, to include teaching and research.

Applications, accompanied by complete curriculum vitae and the names of three references, should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

NORTHAMPTON COLLEGE OF ADVANCED TECHNOLOGY
ST. JOHN STREET, LONDON, E.C.1
DEPARTMENT OF APPLIED PHYSICS

Applications are invited for the post of Assistant Lecturer in Physics, which arises from an increase in establishment. The teaching activities of the Department are primarily concerned with sandwich courses for the Diploma in Technology in Applied Physics together with physics as an ancillary subject for other Diploma in Technology courses. Applicants should possess an honours degree, or an honours diploma in technology in applied physics. It is desirable that applicants should have research or industrial experience in some branch of Applied Physics. The successful candidate will be expected to take part in the research activities of the Department; excellent experimental facilities are available. Salary scale: £930 by £27 10s. to £1,400 per annum. The starting salary will be dependent upon industrial or teaching experience.

Further particulars and a form of application may be obtained from the Secretary.

UNIVERSITY OF OXFORD

Notice is given that Dr. Lee's Professorship of Anatomy will fall vacant on October 1, 1962. The salary will be £3,000 a year plus a departmental allowance of £400 and children's allowances.

The Electors intend to proceed to an election and invite applications in nine copies, naming three referees, but without testimonials, to be received not later than May 4, 1961, by the Registrar, University Registry, Oxford, from whom further particulars may be obtained.

DEPARTMENT OF CHEMICAL ENGINEERING
UNIVERSITY OF BRITISH COLUMBIA
VANCOUVER, B.C., CANADA

Applications are invited for the position of Assistant Professor in the Department of Chemical Engineering. Salary $7,000 (calendar year). This position carries general chemical engineering teaching responsibilities at undergraduate and graduate levels and opportunities for research. An interest in thermodynamics would be particularly desirable.

Applications should be submitted to the Head of the above Department.

NORTHAMPTON COLLEGE OF ADVANCED TECHNOLOGY
ST. JOHN STREET, LONDON, E.C.1
DEPARTMENT OF APPLIED PHYSICS

Applications are invited from graduates or holders of the Diploma in Technology for appointment as Research Assistant to work in one of the following fields: X-ray crystallography, semi-conductors, illumination, electron microscopy, ultrasonics. Successful applicants will be encouraged to submit a thesis for the Membership of the College of Technologists or a Higher Degree. Their duties will include a limited amount of demonstrating in the laboratories. Salary about £500 per annum.

Further particulars may be obtained from the Secretary.

NATIONAL INSTITUTE OF AGRICULTURAL BOTANY

Applications are invited for the posts of Assistant Trials Officers at Leeds University Farm, Headley Hall, Yorks, and at Seale-Hayne Agricultural College, Newton Abbot, Devon. Practical experience in crop production an advantage. Starting salary for men with good honours degree £690, and for others £670, maximum of scale £930; some allowance can be made for postgraduate training. Promotion prospects. Superannuation under F.S.S.U.

Further particulars and application forms from M. G. Tozer, Secretary, N.I.A.B., Huntingdon Road, Cambridge.

INSTITUTE OF NEUROLOGY (QUEEN SQUARE)
DEPARTMENT OF CHEMICAL PATHOLOGY

Research Assistant required, preferably with degree for a psychochemical project. Biochemical experience necessary. Salary in range £615 to £700. Appointment will be for one year in first instance.

Apply to the Secretary, Institute of Neurology, the National Hospital, Queen Square, London, W.C.1.

BROMPTON HOSPITAL
LONDON, S.W.3
HOSPITAL BIOCHEMIST

Applications invited from suitably qualified persons for the post of Non-medical Biochemist (Basic Grade) to work under the direction of the Consultant Clinical Pathologist and Biochemist. Whitley Council conditions of service and salary apply.

Applications should be sent immediately to the House Governor.

KING EDWARD VI SCHOOL
LABORATORY TECHNICIAN (GRADE II)

Applications are invited, from men aged 21 or over, for the post of Laboratory Technician (Grade II) which falls vacant on March 31. Salary is calculated on the scale for miscellaneous officers Grade II (£490 rising by three increments to £555 per annum).

Applications should be sent to the Head Master (Dr. L. John Stroud) at the School, as soon as possible.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Technical Assistant required at Chester Beatty Research Institute, Fulham Road, S.W.3, for haematological and serological work with radiation chimaeras. Ordinary degree graduate, advanced level of education or equivalent required. Previous experience desirable but not essential. Salary on M.R.C. scale according to qualifications within region £750 to £900.—Apply with names of three referees, to the Secretary, 33 Sumner Place, S.W.7, quoting ref.: 301/B/53.

APPLICATIONS ARE INVITED FROM Organic Chemists or Biochemists to assist in a joint research programme in the Departments of Anatomy and Biochemistry on the experimental production of Congenital Malformations. The work will be largely chemical in nature at first, but will become increasingly biochemical as the project advances. Salary up to £1,000 per annum.—Applications to be sent as soon as possible to the Professor of Biochemistry, University College of South Wales and Monmouthshire, Newport Road, Cardiff.

TECHNICIAN MAINLY FOR RESEARCH required in Biology Department, Royal Free Hospital Medical School. Experience in microtechniques advantageous. £595 by £25 to £720, London weighting, superannuation, five weeks' holiday.—Apply with names of two referees as soon as possible to School Secretary, 8 Hunter Street, W.C.1.

RESEARCH ASSISTANT WANTED AT Stoke Mandeville Hospital to help with current research on an immunological project connected with Rheumatoid Arthritis. The person appointed would work directly with the Pathologist undertaking the research. Salary £750 to £1,000 per annum according to qualifications.—Inquiries and applications, giving details of experience and the names of two referees, to the Pathologist, Stoke Mandeville Hospital, Aylesbury, Bucks.

TECHNICAL OFFICER REQUIRED FOR Cyclotron Engineering Section, to gain experience in techniques, to study operation and to take part in development. Qualifications: H.N.C. or degree in electrical or electronic engineering or physics. Experience in R.F. power an advantage. Age under 40. Salary £960 to £1,310, including London Weighting.—Apply, giving full details, to Senior Cyclotron Engineer, Radiotherapeutic Research Unit, Hammersmith Hospital, Ducane Road, London, W.12.

FOR SALE AND WANTED

FOR SALE, 12-IN. REFRACTOR OF EXcellent quality, equatorially mounted with weight-driven clock. Grubb, Dublin, 1874. Inquiries invited.—Box 956, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

TRADE ANNOUNCEMENTS

TUBES FOR SALE—
Several thousand per year

Self-bonded high-grade silicon carbide tubes in 6 in. lengths 35 mm. o./d. and 27 mm. i./d., also 10 mm. o./d. and 6 mm. i./d. approximately. Properties: very hard, high thermal and electrical conductivity, good thermal shock and oxidation resistance at high temperatures.—Box 955, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

BRIGHT'S REMOTE COLD CONTROLLED Microtome (cryostat) custom built for producing frozen sections for rapid diagnostic biopsies.—Full information on request to Bright's Refrigerator Service Ltd., 399 Portobello Road, London, W.10. LADbroke 4153.

MISCELLANEOUS

THE OWNER OF BRITISH PATENT NO. 784,465, entitled "Modified Lanolin" is desirous of entering into negotiations for the grant of licences or otherwise, under suitable terms, for the purpose of exploiting the invention and ensuring its full development and practical working in this country.—For full particulars address George Fuery and Co., 8 Newhall Street, Birmingham 3.

LECTURES AND COURSES

BRADFORD INSTITUTE OF TECHNOLOGY
DEPARTMENT OF CHEMICAL TECHNOLOGY
POSTGRADUATE COURSE IN HIGH POLYMER CHEMISTRY

A postgraduate course in high polymer chemistry leading to an Institute Diploma will be given from October, 1961, to June, 1962. Lectures and practical work cover advanced polymer chemistry and fundamentals of polymer technology. Training in research methods will be given and each student will undertake a supervised research project. The D.S.I.R. has accepted the course as suitable for the tenure of its Advanced Course Studentships. Those attending the course should have a degree in chemistry or the equivalent (G.R.I.C. or H.N.C.).

Further particulars and application forms may be obtained from the Head of the Department of Chemical Technology, Bradford Institute of Technology, Bradford 7.

UNIVERSITY OF LONDON. A LECTURE entitled "Transformation of Carbohydrates in Plants" will be delivered by Professor W. Z. Hassid (California) at 5.30 p.m. on March 21 at the University of London, Senate House, W.C.1. Admission free, without ticket.—James Henderson, Academic Registrar.

NORTHAMPTON COLLEGE OF ADVANCED TECHNOLOGY

ST. JOHN STREET, LONDON, E.C.1

DEPARTMENT OF PRODUCTION TECHNOLOGY AND CONTROL ENGINEERING

ADVERTISEMENT

POSTGRADUATE DIPLOMA COURSE IN INDUSTRIAL AUTOMATIC CONTROL

Eight places are offered in the next Postgraduate Diploma Course in Automatic Control which will start on October 2, 1961. The course is full-time and lasts one academic year. Academic qualification for entry is a degree or Diploma in Technology in Science, Engineering or Mathematics, or an equivalent qualification. Some industrial experience is also required. On successful completion of the course students are awarded the postgraduate Diploma of Northampton College, London. (D.N.C.L.).

Grants may be available for suitable students.

Those interested are invited to apply to the Head of Department of Production Technology and Control Engineering.

LOUGHBOROUGH COLLEGE OF TECHNOLOGY

LEICESTERSHIRE

POSTGRADUATE COURSE IN ERGONOMICS AND CYBERNETICS

Applications are invited for the one year full-time postgraduate course in Ergonomics and Cybernetics which starts October 2, 1961. The course is intended for Engineers and Designers concerned with the development and design of all types of industrial equipment and for graduates in the biological or physical sciences who wish to enter the field of Ergonomics and Cybernetics. Successful completion of the course leads to the award of the Diploma of Associate of Loughborough College of Technology. The course covers basic knowledge of the capabilities and limitations of human beings in the performance of all kinds of work tasks and as operators of machines and control mechanisms. The applications of this knowledge to practical problems in industry is a major objective. The course consists of lectures and seminars, together with practical work, on which there is considerable emphasis, including laboratory studies and some experience in industry. The aim is to impart to students sufficient knowledge to enable them subsequently to undertake work in industry in this field. Postgraduate awards, covering tuition fees, board residence in Hall and a personal grant are available.

Further particulars and forms of application for registration can be obtained from the Head of the Department of Ergonomics and Cybernetics, College of Technology, Loughborough, Leicestershire.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3

DEPARTMENT OF PHYSICS

POSTGRADUATE COURSE IN SOLID STATE PHYSICS

Application is invited from graduates in Physics or holders of Diplomas in Technology for admission to a one-year full-time postgraduate course in Solid State Physics beginning in September, 1961.

The course is approved by the D.S.I.R. for the tenure of Advanced Course Studentships and suitably qualified students may be registered for the M.Sc. degree of the University of London.

Further information and application forms may be obtained from the Secretary (Telephone No. FLA 5747).

UNIVERSITY OF LONDON: A LECTURE entitled "Spectrum of Waves and Sea Level Variations" will be delivered by Dr. G. E. R. Deacon (National Institute of Oceanography, Wormley) at 5.30 p.m. on March 21 at Imperial College of Science and Technology (Main Geology Lecture Theatre, Royal School of Mines), Prince Consort Road, S.W.7. Admission free, without ticket.—James Henderson, Academic Registrar.

GRANTS & SCHOLARSHIPS

LOUGHBOROUGH COLLEGE OF TECHNOLOGY

LEICESTERSHIRE

NUFFIELD POSTGRADUATE STUDENTSHIPS IN ERGONOMICS

Applications are invited for four postgraduate studentships provided by the Nuffield Foundation to enable graduates in science, engineering or technology (or diplomates of graduate status), to attend the One Year Full-time Postgraduate Course in Ergonomics and Cybernetics which starts October 2, 1961, in the Department of Ergonomics and Cybernetics. Applicants should preferably have had at least one to two years' industrial experience in a field such as product or process design, factory operation or layout, systems design, work study or production management, in which human factor problems are important. The value of the Nuffield Studentships normally ranges from £750 to approximately £1,200, and exceptionally to £1,500. Allowance is made for the marital status of the applicant and size of family. The value of an award will be adjusted in consultation with the applicant's employer to take into account any financial support which the employer may wish to give to the applicant during his tenure of the award.

Forms of application for the Nuffield postgraduate studentships may be obtained from the Academic Registrar, College of Technology, Loughborough, Leicestershire, to whom completed forms should be returned as soon as possible.

Full particulars of the Course in Ergonomics and Cybernetics may be obtained from the Head of the Department of Ergonomics and Cybernetics.

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF PHYSICS AND ELECTRONICS

Applications are invited for a Research Studentship supported by the United Kingdom Atomic Energy Authority, for work in an interesting new field of nuclear magnetic resonance in ferromagnetic materials. The research work will be carried out jointly in the Departments of Physics and Electronics. Applicants should have an honours degree in physics or electronic engineering and will be encouraged to submit their work for a higher degree. Tenure is for three years and the salary scale is £600 plus demonstrating fees.

Applications, including full details of qualifications and the names of two referees, should be sent to the Secretary and Registrar, University of Southampton.

UNIVERSITY OF EDINBURGH

STUDENTSHIPS AND FELLOWSHIPS

Studentships and Junior and Senior Fellowships, open to graduates of any University and tenable in the Faculties of Divinity, Law, Medicine, Arts, Science and Music of the University of Edinburgh, will be available for award in session 1961-62. Up to six awards may be made. The value of a Postgraduate Studentship is £300; if renewed for a second and third year £320 and £340 respectively. The value of a Junior Fellowship is £500; if renewed for a second and third year £550 and £600 respectively. The value of a Senior Fellowship is £750; if renewed for a second and third year £800 and £850 respectively. Applications must be submitted through the Dean of the appropriate Faculty before April 15, 1961.

Further particulars and application forms may be obtained from the Secretary to the University, Old College, South Bridge, Edinburgh, 8.

CHARLES H. STEWART,
Secretary to the University.

THE COUNCIL OF THE ROYAL COLLEGE of Veterinary Surgeons Trust announce the following Scholarship of the Trust: The International League for the Protection of Horses Scholarship for Research in Equine Health Promotion. Value £850 per annum.—Further details from the Secretary, R.C.V.S. Trust, College House, 29-31 Wright's Lane, London, W.8. Closing date for receipt of applications is May 15, 1961.

NORTHAMPTON COLLEGE OF ADVANCED TECHNOLOGY

ST. JOHN STREET, LONDON, E.C.1

DEPARTMENT OF PRODUCTION TECHNOLOGY AND CONTROL ENGINEERING

POSTGRADUATE RESEARCH IN INSTRUMENT AND CONTROL ENGINEERING

Facilities are available in this Department for research in Instrument and Control Engineering leading to a higher degree of the University of London or Membership of the College of Technologists (M.C.T.).

Grants may be available for suitable students.

Those interested are invited to apply to the Head of Department of Production Technology and Control Engineering.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for Research Studentships for the Session 1961-62. These studentships of the value of £340 per annum are tenable for one year in the first instance, with possible extension for a second year. Research Studentships may be awarded in any of the following subjects: Mathematics, Physics, Chemistry, Biology, Geology, Communication. Candidates (men or women) should have a good honours degree of a British university but applications from students who expect to graduate in 1961 will also be considered.

Application forms may be obtained from the Registrar, the College, Keele, Staffs, to whom completed forms should be returned not later than May 31, 1961.

ANIMAL HEALTH TRUST

RESEARCH TRAINING SCHOLARSHIPS 1961

A few Research Training Scholarships are offered by the Animal Health Trust to recent Graduates in Veterinary Medicine or Natural Science. These Scholarships to the value of £500 per annum will be exempt from income tax and will carry a grant not exceeding £60 per annum towards the payment of essential fees. Applicants must be desirous of entering upon a research career connected with Veterinary Medicine.

Forms of application can be obtained from The Scientific Director, The Animal Health Trust, 14 Ashley Place, London, S.W.1. The closing date for the receipt of applications is May 12, 1961.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

A Bursary is available from October 1, 1961 (or earlier) for research on the chemistry and metallurgy of the attack of highly alloyed steels by molten oxides. Work suitable for a graduate in chemistry or metallurgy wishing to proceed to a higher degree. Value approximately £400 per annum plus fees.

Applications, with summary of career and names of referees, to Dr. D. A. Pantony, Metallurgy Dept., Imperial College, London, S.W.7.

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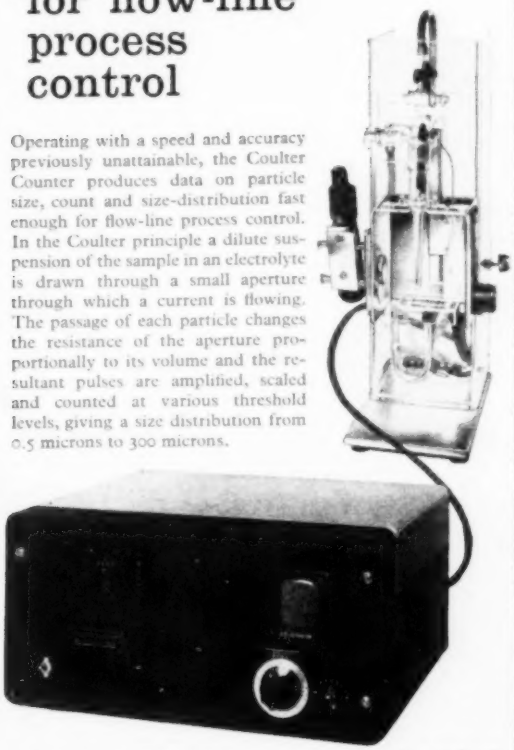

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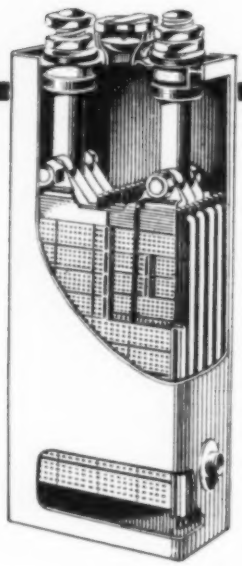

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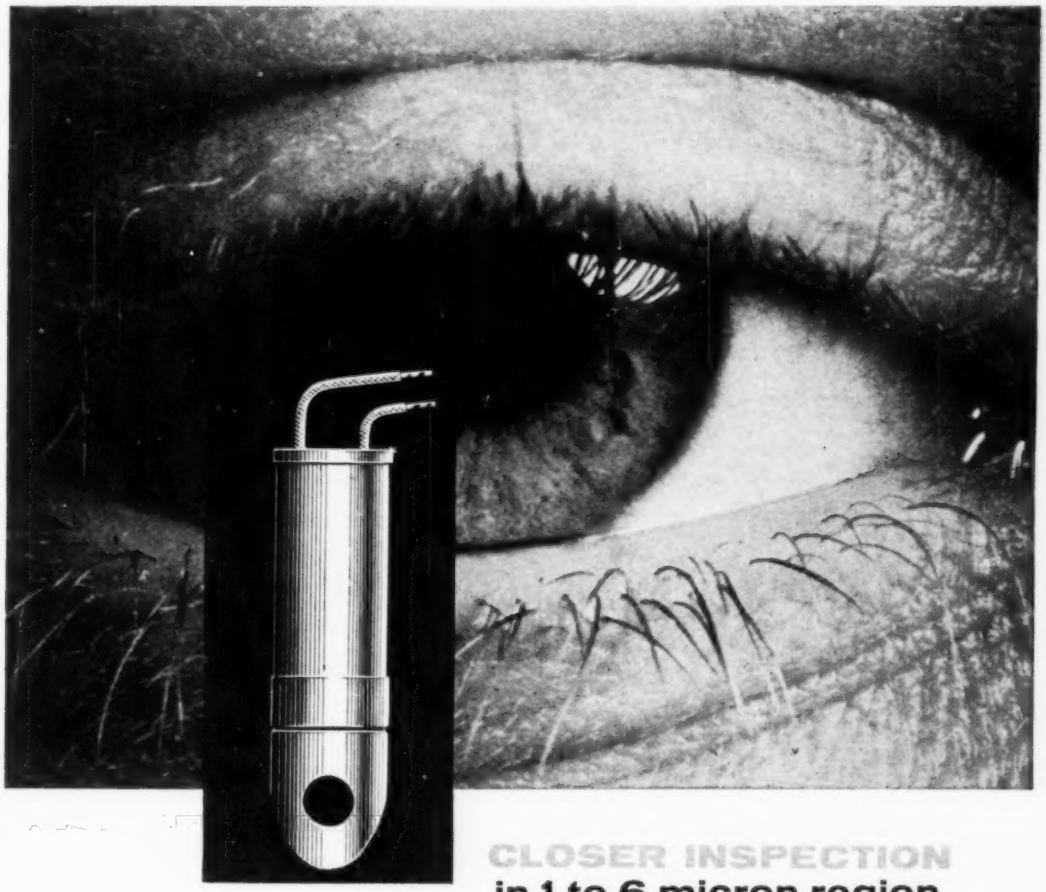

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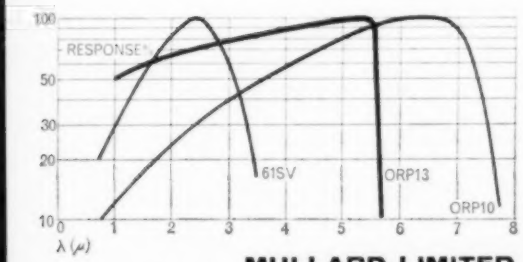

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